heterocyclic refers to a nonaromatic cyclic group wherein there is at least one heteroatom, such as oxygen, sulfur, nitrogen or phosphorus in the ring. Nonlimiting examples of heteroaryl and heterocyclic groups include furyl, furanyl, pyridyl, pyrimidyl, thienyl, isothiazolyl, imidazolyl, tetrazolyl, pyrazinyl, benzofuranyl, benzothiophenyl, quinolyl, isoquinolyl, benzothienyl, isobenzofuryl, pyrazolyl, indolyl, isoindolyl, benzimidazolyl, purinyl, carbazolyl, oxazolyl, thiazolyl, isothiazolyl, 1,2,4-thiadiazolyl, isooxazolyl, pyrrolyl, quinazolinyl, cinnolinyl, phthalazinyl, xanthinyl, hypoxanthinyl, thiophene, furan, pyrrole, isopyrrole, pyrazole, or imidazole. The heteroaromatic group can be optionally substituted as described above for aryl. The heterocyclic group can be optionally substituted with one or more moieties selected from the group consisting of alkyl, halo, haloalkyl, hydroxyl, carboxyl, acyl, acyloxy, amino, amido, carboxyl derivatives, alkylamino, dialkylamino, arylamino, alkoxy, aryloxy, nitro, cyano, sulfonic acid, thiol, imine, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, ester, carboxylic acid, amide, phosphonyl, phosphinyl, phosphoryl, phosphine, thioester, thioether, acid halide, anhydride, oxime, hydrozine, carbamate, phosphonic acid, phosphonate, or any other viable functional group that does not inhibit the pharmacological activity of this compound, either unprotected, or protected as necessary, as known to those skilled in the art, for example, as taught in Greene, *et al.*, Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991, hereby incorporated by reference. The heteroaromatic can be partially or totally hydrogenated as desired. As a nonlimiting example, dihydropyridine can be used in place of pyridine. Functional oxygen and nitrogen groups on the heteroaryl group can be protected as necessary or desired. Suitable protecting groups are well known to those skilled in the art, and include trimethylsilyl, dimethylhexylsilyl, *t*-butyldimethylsilyl, and *t*-butyldiphenylsilyl, trityl or substituted trityl, alkyl groups, acyl groups such as acetyl and propionyl, methanesulfonyl, and p-toluenesulfonyl.

The term amino acid includes naturally occurring and synthetic amino acids, and includes but is not limited to, alanyl, valinyl, leucinyl, isoleuccinyl, prolinyl, phenylalaninyl, tryptophanyl, methioninyl, glycinyl, serinyl, threoninyl, cysteinyl, tyrosinyl, asparaginyl, glutaminyl, aspartoyl, glutaroyl, lysinyl, argininyl and histidinyl.

The term "ether," as used herein, refers to oxygen that is disubstituted with independent alkyl groups or two alkyl groups that together formed a ring or a bridge. Some non-limiting examples include 4-(tetrahydrobenzimidazol-1-yl)butoxy, 5-(tetra-

hydrobenzimidazol-1-yl)pentoxy, ethoxy, n-propoxy or isoproproxy. The ethers also can be optionally substituted with one or more moieties selected from the group consisting of alkyl, halo, haloalkyl, hydroxyl, carboxyl, acyl, acyloxy, amino, amido, carboxyl derivatives, alkylamino, dialkylamino, arylamino, alkoxy, aryloxy, nitro, cyano, sulfonic acid, thiol, imine, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, ester, carboxylic acid, amide, phosphonyl, phosphinyl, phosphoryl, phosphine, thioester, thioether, acid halide, anhydride, oxime, hydrozine, carbamate, phosphonic acid, phosphonate, or any other viable functional group that does not inhibit the pharmacological activity of this compound, either unprotected, or protected as necessary, as known to those skilled in the art, for example, as taught in Greene, *et al.*, Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991, hereby incorporated by reference.

The term "amide," as used herein, refers to a carbonyl moiety wherein the non-alkyl moiety is formed from an amine. Some non-limiting examples are formylamino, acetylamino, propionylamino, butanoylamino, isobutanoylamino, pentanoylamino, 3-methyl-butanoylamino, hexanoylamino, methoxycarbonylamino, ethoxycarbonylamino, n-propoxycarbonylamino, isopropoxycarbonylamino, benzamido, cyclopentylcarbonyl-amido, cyclohexylcarbonylamido, cycloheptylcarbonyl-amido, phenylacetylamido, hydrozine, carbamate, phosphonic acid, phosphonate, or any other viable functional group that does not inhibit the pharmacological activity of this compound, either unprotected, or protected as necessary, as known to those skilled in the art, for example, as taught in Greene, *et al.*, Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991, hereby incorporated by reference.

The term "sulfamoyl" is a hexavalent sulfur covalently bound to at least two oxygens and a nitrogen. Some non-limiting examples include methanesulphonylamino, ethanesulphonylamino, n-propanesulphonylamino, isopropanesulphonylamino, n-butane-sulphonylamino, N-ethyl-phenylmethanesulphonylamido, N-ethyl-2-phenylethane-sulphonylamido, N-ethyl-3-phenylpropanesulphonylamido, N-ethyl-naphthalen-1-yl-sulphonamido or N-ethyl-naphthalen-2-yl-sulphonylamido. The sulfamoyl group also can be optionally substituted with one or more moieties selected from the group consisting of alkyl, halo, haloalkyl, hydroxyl, carboxyl, acyl, acyloxy, amino, amido, carboxyl derivatives, alkylamino, dialkylamino, arylamino, alkoxy, aryloxy, nitro, cyano, sulfonic acid, thiol, imine, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, ester, carboxylic acid, amide, phosphonyl, phosphinyl, phosphoryl, phosphine, thioester, thioether, acid halide,

anhydride, oxime, hydrozine, carbamate, phosphonic acid, phosphonate, or any other viable functional group that does not inhibit the pharmacological activity of this compound, either unprotected, or protected as necessary, as known to those skilled in the art, for example, as taught in Greene, *et al.*, Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991, hereby incorporated by reference.

The term "thio" refers to a sulfur covalently bound to a hydrogen or a carbon based group. Some non-limiting examples include methylmercapto, ethylmercapto, n-propylmercapto, isopropylmercapto or n-butylmercapto, ethylthio, n-propylthio or isopropylthio group. The thio group also can be optionally substituted with one or more moieties selected from the group consisting of alkyl, halo, haloalkyl, hydroxyl, carboxyl, acyl, acyloxy, amino, amido, carboxyl derivatives, alkylamino, dialkylamino, arylamino, alkoxy, aryloxy, nitro, cyano, sulfonic acid, thiol, imine, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, ester, carboxylic acid, amide, phosphonyl, phosphinyl, phosphoryl, phosphine, thioester, thioether, acid halide, anhydride, oxime, hydrozine, carbamate, phosphonic acid, phosphonate, or any other viable functional group that does not inhibit the pharmacological activity of this compound, either unprotected, or protected as necessary, as known to those skilled in the art, for example, as taught in Greene, *et al.*, Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991, hereby incorporated by reference.

The term "ester" refers to a carbonyl flanked by an alkoxy group and a carbon based group. Some non-limiting examples include hydroxycarbonyl, methoxycarbonyl, ethoxycarbonyl, n-propyloxycarbonyl, isopropyloxycarbonyl, n-butyloxycarbonyl, isobutyloxycarbonyl, tert-butyloxycarbonyl or 1-(cinnamyloxycarbonyloxy)-ethoxy-carbonyl. The ester group also can be optionally substituted with one or more moieties selected from the group consisting of alkyl, halo, haloalkyl, hydroxyl, carboxyl, acyl, acyloxy, amino, amido, carboxyl derivatives, alkylamino, dialkylamino, arylamino, alkoxy, aryloxy, nitro, cyano, sulfonic acid, thiol, imine, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, ester, carboxylic acid, amide, phosphonyl, phosphinyl, phosphoryl, phosphine, thioester, thioether, acid halide, anhydride, oxime, hydrozine, carbamate, phosphonic acid, phosphonate, or any other viable functional group that does not inhibit the pharmacological activity of this compound, either unprotected, or protected as necessary, as known to those skilled in the art, for example, as taught in Greene, *et al.*,

Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991, hereby incorporated by reference.

The term "urethane" or "carbamate" refers to $-OC(O)NR^4R^5$ in which R^4 and R^5 are independently selected from straight, branched, or cyclic alkyl or lower alkyl, alkoxyalkyl including methoxymethyl, aralkyl including benzyl, aryloxyalkyl such as phenoxymethyl, aryl including phenyl optionally substituted with halogen, C_1 to C_4 alkyl or C_1 to C_4 alkoxy, sulfonate esters such as alkyl or aralkyl sulphonyl including methanesulfonyl, the mono, di or triphosphate ester, trityl or monomethoxytrityl, substituted benzyl, trialkylsilyl (e.g. dimethyl-*t*-butylsilyl) or diphenylmethylsilyl. Aryl groups in the carbamide optimally comprise a phenyl group. The term "lower carbamide" refers to an carbamide group in which the non-carbonyl moiety is a lower alkyl. The carbamide group also can be optionally substituted with one or more moieties selected from the group consisting of alkyl, halo, haloalkyl, hydroxyl, carboxyl, acyl, acyloxy, amino, amido, carboxyl derivatives, alkylamino, dialkylamino, arylamino, alkoxy, aryloxy, nitro, cyano, sulfonic acid, thiol, imine, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, ester, carboxylic acid, amide, phosphonyl, phosphinyl, phosphoryl, phosphine, thioester, thioether, acid halide, anhydride, oxime, hydrozine, carbamate, phosphonic acid, phosphonate, or any other viable functional group that does not inhibit the pharmacological activity of this compound, either unprotected, or protected as necessary, as known to those skilled in the art, for example, as taught in Greene, *et al.*, Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991, hereby incorporated by reference.

The term carbohydrate, used herein refers to mono, di, tri, oligo, and poly saccharides consisting of furanose and pyranose sugars such as threose, ribulose, ketose, gentiobiose, aldose, aldotetrose, aldopentose, aldohexose, ketohexose, ketotetrose, ketopentose, erythrose, threose, ribose, deoxyribose, arabinose, xylose, lyxose, allose, altrose, glucose, mannose, gulose, idose, glactose, talose, erythrulose, ribulose, xylulose, psicose, fructose, sorbose, tagatose, dextrose, maltose, lactose, sucrose, or cellulose. The carbohydrate moiety as disclosed herein can be optionally substituted with one or more moieties selected from the group consisting of alkyl, halo, haloalkyl, hydroxyl, carboxyl, acyl, acyloxy, amino, amido, carboxyl derivatives, alkylamino, dialkylamino, arylamino, alkoxy, aryloxy, nitro, cyano, sulfonic acid, thiol, imine, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, ester, carboxylic acid, amide, phosphonyl, phosphinyl, phosphoryl,

phosphine, thioester, thioether, acid halide, anhydride, oxime, hydrozine, carbamate, phosphonic acid, phosphonate, or any other viable functional group that does not inhibit the pharmacological activity of this compound, either unprotected, or protected as necessary, as known to those skilled in the art, for example, as taught in Greene, *et al.*, Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991, hereby incorporated by reference.

The term alkylheteroaryl refers to an alkyl group substituted by a heteroaryl substituent.

The term host, as used herein, refers to a multicellular organism in which the symptoms of an autoimmune or inflammatory disorder, including animals, and preferably a human. The term host specifically refers to animals, in particular, primates (including chimpanzees) and humans, in which autoimmune and inflammatory disorders occur. In most animal applications of the present invention, the host is a human patient. Veterinary applications, in certain indications, however, are clearly anticipated by the present invention (such as chimpanzees).

III. Pharmaceutically Acceptable Salt Formulations

Modifications of the active compound can affect the bioavailability and rate of metabolism of the active species, thus providing control over the delivery of the active species. Further, the modifications can affect the activity of the compound, in some cases increasing the activity over the parent compound. This can easily be assessed by preparing the derivative and testing its activity according to the methods described herein, or other method known to those skilled in the art.

In cases where compounds are sufficiently basic or acidic to form stable nontoxic acid or base salts, administration of the compound as a pharmaceutically acceptable salt may be appropriate. The term "pharmaceutically acceptable salts" or "complexes" refers to salts or complexes that retain the desired biological activity of the compounds of the present invention and exhibit minimal undesired toxicological effects.

Examples of pharmaceutically acceptable salts are organic acid addition salts formed with acids, which form a physiological acceptable anion, for example, tosylate,

methanesulfonate, acetate, citrate, malonate, tartarate, succinate, benzoate, ascorbate, α-ketoglutarate and α-glycerophosphate. Suitable inorganic salts may also be formed, including, sulfate, nitrate, bicarbonate and carbonate salts. Alternatively, the pharmaceutically acceptable salts may be made with sufficiently basic compounds such as an amine with a suitable acid affording a physiologically acceptable anion. Alkali metal (for example, sodium, potassium or lithium) or alkaline earth metal (for example calcium) salts of carboxylic acids can also be made.

Nonlimiting examples of such salts are (a) acid addition salts formed with inorganic acids (for example, hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, nitric acid, and the like), and salts formed with organic acids such as acetic acid, oxalic acid, tartaric acid, succinic acid, malic acid, ascorbic acid, benzoic acid, tannic acid, pamoic acid, alginic acid, polyglutamic acid, naphthalenesulfonic acid, naphthalenedisulfonic acid, and polygalcturonic acid; (b) base addition salts formed with metal cations such as zinc, calcium, bismuth, barium, magnesium, aluminum, copper, cobalt, nickel, cadmium, sodium, potassium, and the like, or with a cation formed from ammonia, N,N-dibenzylethylenediamine, D-glucosamine, tetraethylammonium, or ethylenediamine; or (c) combinations of (a) and (b); e.g., a zinc tannate salt or the like. Also included in this definition are pharmaceutically acceptable quaternary salts known by those skilled in the art, which specifically include the quaternary ammonium salt of the formula $-NR^+A^-$, wherein R is as defined above and A is a counterion, including chloride, bromide, iodide, -O-alkyl, toluenesulfonate, methylsulfonate, sulfonate, phosphate, or carboxylate (such as benzoate, succinate, acetate, glycolate, maleate, malate, citrate, tartrate, ascorbate, benzoate, cinnamoate, mandeloate, benzyloate, and diphenylacetate).

Pharmaceutically acceptable prodrugs refer to a compound that is metabolized, for example hydrolyzed or oxidized, in the host to form the compound of the present invention. Typical examples of prodrugs include compounds that have biologically labile protecting groups on a functional moiety of the active compound. Prodrugs include compounds that can be oxidized, reduced, aminated, deaminated, hydroxylated, dehydroxylated, hydrolyzed, dehydrolyzed, alkylated, dealkylated, acylated, deacylated, phosphorylated, dephosphorylated to produce the active compound. The compounds of this invention possess anti-inflammatory activity, or are metabolized to a compound that exhibits such activity.

Any of the compounds described herein can be administered as a prodrug to increase the activity, bioavailability, stability or otherwise alter the properties of the compound. A number of prodrug ligands are known. In general, alkylation, acylation or other lipophilic modification of the compound will increase the stability of the compound. Examples of substituent groups that can replace one or more hydrogens on the compound are alkyl, aryl, steroids, carbohydrates, including sugars, 1,2-diacylglycerol and alcohols. Many are described in R. Jones and N. Bischofberger, *Antiviral Research*, 27 (1995) 1-17. Any of these can be used in combination with the disclosed compounds to achieve a desired effect.

IV. Autoimmune and Inflammatory Diseases

The compounds of the present invention can be used to treat any disorder that is mediated by LO. Dysfunction in LO production is implicated in a wide variety of disease states, including but not limited to arthritis, asthma, dermatitis, psoriasis, cystic fibrosis, post transplantation late and chronic solid organ rejection, multiple sclerosis, systemic lupus erythematosis, inflammatory bowel diseases, autoimmune diabetes, diabetic retinopathy, rhinitis, ischemia-reperfusion injury, post-angioplasty restenosis, chronic obstructive pulmonary disease (COPD), glomerulonephritis, Graves disease, gastrointestinal allergies, and conjunctivitis.

Nonlimiting examples of arthritis include rheumatoid (such as soft-tissue rheumatism and non-articular rheumatism, fibromyalgia, fibrositis, muscular rheumatism, myofascil pain, humeral epicondylitis, frozen shoulder, Tietze's syndrome, fascitis, tendinitis, tenosynovitis, bursitis), juvenile chronic, spondyloarthropaties (ankylosing spondylitis), osteoarthritis, hyperuricemia and arthritis associated with acute gout, chronic gout and systemic lupus erythematosus.

Human endothelial disorders mediated by LO include psoriasis, eczematous dermatitis, Kaposi's sarcoma as well as proliferative disorders of smooth muscle cells.

In yet another embodiment, the compounds disclosed herein can be selected to treat anti-inflammatory conditions that are mediated by mononuclear leukocytes.

In one embodiment, the compounds of the present invention are selected for the prevention or treatment of tissue or organ transplant rejection. Treatment and prevention of organ or tissue transplant rejection includes, but are not limited to treatment of recipients of heart, lung, combined heart-lung, liver, kidney, pancreatic, skin, spleen, small bowel, or corneal transplants. The compounds can also be used in the prevention or treatment of graft-versus-host disease, such as sometimes occurs following bone marrow transplantation.

V. Combination and Alternation Therapy

Any of the compounds disclosed herein can be administered in combination or alternation with a second biologically active agent to increase its effectiveness against the target disorder.

In combination therapy, effective dosages of two or more agents are administered together, whereas during alternation therapy an effective dosage of each agent is administered serially. The dosages will depend on absorption, inactivation and excretion rates of the drug as well as other factors known to those of skill in the art. It is to be noted that dosage values will also vary with the severity of the condition to be alleviated. It is to be further understood that for any particular subject, specific dosage regimens and schedules should be adjusted over time according to the individual need and the professional judgment of the person administering or supervising the administration of the compositions.

The efficacy of a drug can be prolonged, augmented, or restored by administering the compound in combination or alternation with a second, and perhaps third, agent that induces a different biological pathway from that caused by the principle drug. Alternatively, the pharmacokinetics, biodistribution or other parameter of the drug can be altered by such combination or alternation therapy. In general, combination therapy is typically preferred over alternation therapy because it induces multiple simultaneous stresses on the condition.

Any method of alternation can be used that provides treatment to the patient. Nonlimiting examples of alternation patterns include 1-6 weeks of administration of an effective amount of one agent followed by 1-6 weeks of administration of an effective

amount of a second agent. The alternation schedule can include periods of no treatment. Combination therapy generally includes the simultaneous administration of an effective ratio of dosages of two or more active agents.

Illustrative examples of specific agents that can be used in combination or alternation with the compounds of the present invention are described below in regard to asthma and arthritis. The agents set out below or others can alternatively be used to treat a host suffering from any of the other disorders listed in Section IV or that are mediated by LO, and preferably 15-LO.

Asthma

In one embodiment, the compound of the present invention is administered in combination or alternation with heparin, frusemide, ranitidine, an agent that effects respiratory function, such as DNAase, or immunosuppressive agents, IV gamma globulin, troleandomycin, cyclosporin (Neoral), methotrexate, FK-506, gold compounds such as Myochrysine (gold sodium thiomalate), platelet activating factor (PAF) antagonists such as thromboxane inhibitors, leukotriene-D_4-receptor antagonists such as Accolate (zafirlukast), Ziflo (zileuton), leukotriene C_1 or C_2 antagonists and inhibitors of leukotriene synthesis such as zileuton for the treatment of asthma, or an inducible nitric oxide synthase inhibitor.

In another embodiment, the active compound is administered in combination or alternation with one or more other prophylactic agent(s). Examples of prophylactic agents that can be used in alternation or combination therapy include but are not limited to sodium cromoglycate, Intal (cromolyn sodium, Nasalcrom, Opticrom, Crolom, Ophthalmic Crolom), Tilade (nedocromil, nedocromil sodium) and ketotifen.

In another embodiment, the active compound is administered in combination or alternation with one or more other β_2-adrenergic agonist(s) (β agonists). Examples of β_2-adrenergic agonists (β agonists) that can be used in alternation or combination therapy include but are not limited to albuterol (salbutamol, Proventil, Ventolin), terbutaline, Maxair (pirbuterol), Serevent (salmeterol), epinephrine, metaproterenol (Alupent, Metaprel), Brethine (Bricanyl, Brethaire, terbutaline sulfate), Tornalate (bitolterol), isoprenaline, ipratropium bromide, bambuterol hydrochloride, bitolterol mesylate,

broxaterol, carbuterol hydrochloride, clenbuterol hydrochloride, clorprenaline hydrochloride, efirmoterol fumarate, ephedra (source of alkaloids), ephedrine (ephedrine hydrochloride, ephedrine sulfate), etafedrine hydrochloride, ethylnoradrenaline hydrochloride, fenoterol hydrochloride, hexoprenaline hydrochloride, isoetharine hydrochloride, isoprenaline, mabuterol, methoxyphenamine hydrochloride, methylephedrine hydrochloride, orciprenaline sulphate, phenylephrine acid tartrate, phenylpropanolamine (phenylpropanolamine polistirex, phenylpropanolamine sulphate), pirbuterol acetate, procaterol hydrochloride, protokylol hydrochloride, psuedoephedrine (psuedoephedrine polixtirex, psuedoephedrine tannate, psuedoephedrine hydrochloride, psuedoephedrine sulphate), reproterol hydrochloride, rimiterol hydrobromide, ritodrine hydrochloride, salmeterol xinafoate, terbutaline sulphate, tretoquinol hydrate and tulobuterol hydrochloride.

In another embodiment, the active compound is administered in combination or alternation with one or more other corticosteriod(s). Examples of corticosteriods that can be used in alternation or combination therapy include but are not limited to glucocorticoids (GC), Aerobid (Aerobid-M, flunisolide), Azmacort (triamcinolone acetonide), Beclovet (Vanceril, beclomethasone dipropionate), Flovent (fluticasone), Pulmicort (budesonide), prednisolone, hydrocortisone, adrenaline, Alclometasone Dipropionate, Aldosterone, Amcinonide, Beclomethasone Dipropionate, Bendacort, Betamethasone (Betamethasone Acetate, Betamethasone Benzoate, Betamethasone Dipropionate, Betamethasone Sodium Phosphate, Betamethasone Valerate), Budesonide, Ciclomethasone, Ciprocinonide, Clobetasol Propionate, Clobetasone Butyrate, Clocortolone Pivalate, Cloprednol, Cortisone Acetate, Cortivazol, Deflazacort, Deoxycortone Acetate (Deoxycortone Pivalate), Deprodone, Desonide, Desoxymethasone, Dexamethasone (Dexamethasone Acetate, Dexamethasone Isonicotinate, Dexamethasone Phosphate, Dexamethasone Sodium Metasulphobenzoate, Dexamethasone Sodium Phosphate), Dichlorisone Acetate, Diflorasone Diacetate, Diflucortolone Valerate, Difluprednate, Domoprednate, Endrysone, Fluazacort, Fluclorolone Acetonide, Fludrocortisone Acetate, Flumethasone (Flumethasone Pivalate), Flunisolide, Flucinolone Acetonide, Fluocinonide, Fluocortin Butyl, Fluocortolone (Fluocortolone Hexanoate, Fluocortolone Pivalate), Fluorometholone (Fluorometholone Acetate), Fluprednidene Acetate, Fluprednisolone, Flurandrenolone, Fluticasone Propionate, Formocortal, Halcinonide, Halobetasol Propionate, Halometasone, Hydrocortamate Hydrochloride, Hydrocortisone (Hydrocortisone Acetate, Hydrocortisone

Butyrate, Hydrocortisone Cypionate, Hydrocortisone Hemisuccinate, Hydrocortisone Sodium Phosphate, Hydrocortisone Sodium Succinate, Hydrocortisone Valerate), Medrysone, Meprednisone, Methylprednisolone (Methylprednisolone Acetate, Methylprednisolone ,Hemisuccinate, Methylprednisolone Sodium Succinate), Mometasone Furoate, Paramethasone Acetate, Prednicarbate, Prednisolamate Hydrochloride, Prednisolone (Prednisolone Acetate, Prednisolone Hemisuccinate, Prednisolone Hexanoate, Prednisolone Pivalate, Prednisolone Sodium Metasulphobenzoate, Prednisolone Sodium Phosphate, Prednisolone Sodium Succinate, Prednisolone Steaglate, Prednisolone Tebutate), Prednisone (Prednisone Acetate), Prednylidene, Procinonide, Rimexolone, Suprarenal Cortex, Tixocortol Pivalate, Triamcinolone (Triamcinolone Acetonide, Triamcinolone Diacetate and Triamcinolone Hexacetonide).

In another embodiment, the active compound is administered in combination or alternation with one or more other antihistamine(s) (H_1 receptor antagonists). Examples of antihistamines (H_1 receptor antagonists) that can be used in alternation or combination therapy include alkylamines, ethanolamines, ethylenediamines, piperazines, piperidines or phenothiazines. Some non-limiting examples of antihistamines are Chlortrimeton (Teldrin, chlorpheniramine), Atrohist (brompheniramine, Bromarest, Bromfed, Dimetane), Actidil (triprolidine), Dexchlor (Poladex, Polaramine, dexchlorpheniramine), Benadryl (diphen-hydramine), Tavist (clemastine), Dimetabs (dimenhydrinate, Dramamine, Marmine), PBZ (tripelennamine), pyrilamine, Marezine (cyclizine), Zyrtec (cetirizine), hydroxyzine, Antivert (meclizine, Bonine), Allegra (fexofenadine), Hismanal (astemizole), Claritin (loratadine), Seldane (terfenadine), Periactin (cyproheptadine), Nolamine (phenindamine, Nolahist), Phenameth (promethazine, Phenergan), Tacaryl (methdilazine) and Temaril (trimeprazine).

Alternatively, the compound of the present invention is administered in combination or alternation with

(a) xanthines and methylxanthines, such as Theo-24 (theophylline, Slo-Phylline, Uniphyllin, Slobid, Theo-Dur), Choledyl (oxitriphylline), aminophylline;

(b) anticholinergic agents (antimuscarinic agents) such as belladonna alkaloids, Atrovent (ipratropium bromide), atropine, oxitropium bromide;

(c) phosphodiesterase inhibitors such as zardaverine;

(d) calcium antagonists such as nifedipine; or

(e) potassium activators such as cromakalim for the treatment of asthma.

Arthritic disorders

In one embodiment, the compound of the present invention can also be administered in combination or alternation with apazone, amitriptyline, chymopapain, collegenase, cyclobenzaprine, diazepam, fluoxetine, pyridoxine, ademetionine, diacerein, glucosamine, hylan (hyaluronate), misoprostol, paracetamol, superoxide dismutase mimics, TNFα receptor antagonists, TNFα antibodies, P38 Kinase inhibitors, tricyclic antidepressents, cJun kinase inhibitors or immunosuppressive agents, IV gamma globulin, troleandomycin, cyclosporin (Neoral), methotrexate, FK-506, gold compounds such as Myochrysine (gold sodium thiomalate), platelet activating factor (PAF) antagonists such as thromboxane inhibitors, leukotriene-D_4-receptor antagonists such as Accolate (zafirlukast), Ziflo (zileuton), leukotriene C_1, C_2 antagonists and inhibitors of leukotriene synthesis such as zileuton for the treatment of arthritic disorders, inducible nitric oxide sythase inhibitors.

In another embodiment, the active compound is administered in combination or alternation with one or more other corticosteriod(s). Examples of corticosteriods that can be used in alternation or combination therapy include but are not limited to glucocorticoids (GC), Aerobid (Aerobid-M, flunisolide), Azmacort (triamcinolone acetonide), Beclovet (Vanceril, beclomethasone dipropionate), Flovent (fluticasone), Pulmicort (budesonide), prednisolone, hydrocortisone, adrenaline, Alclometasone Dipropionate, Aldosterone, Amcinonide, Beclomethasone Dipropionate, Bendacort, Betamethasone (Betamethasone Acetate, Betamethasone Benzoate, Betamethasone Dipropionate, Betamethasone Sodium Phosphate, Betamethasone Valerate), Budesonide, Ciclomethasone, Ciprocinonide, Clobetasol Propionate, Clobetasone Butyrate, Clocortolone Pivalate, Cloprednol, Cortisone Acetate, Cortivazol, Deflazacort, Deoxycortone Acetate (Deoxycortone Pivalate), Deprodone, Desonide, Desoxymethasone, Dexamethasone (Dexamethasone Acetate, Dexamethasone Isonicotinate, Dexamethasone Phosphate, Dexamethasone Sodium Metasulphobenzoate, Dexamethasone Sodium Phosphate), Dichlorisone Acetate, Diflorasone Diacetate, Diflucortolone Valerate, Difluprednate, Domoprednate, Endrysone,

Fluazacort, Fluclorolone Acetonide, Fludrocortisone Acetate, Flumethasone (Flumethasone Pivalate), Flunisolide, Fluocinolone Acetonide, Fluocinonide, Fluocortin Butyl, Fluocortolone (Fluocortolone Hexanoate, Fluocortolone Pivalate), Fluorometholone (Fluorometholone Acetate), Fluprednidene Acetate, Fluprednisolone, Flurandrenolone, Fluticasone Propionate, Formocortal, Halcinonide, Halobetasol Propionate, Halometasone, Hydrocortamate Hydrochloride, Hydrocortisone (Hydrocortisone Acetate, Hydrocortisone Butyrate, Hydrocortisone Cypionate, Hydrocortisone Hemisuccinate, Hydrocortisone Sodium Phosphate, Hydrocortisone Sodium Succinate, Hydrocortisone Valerate), Medrysone, Meprednisone, Methylprednisolone (Methylprednisolone Acetate, Methylprednisolone ,Hemisuccinate, Methylprednisolone Sodium Succinate), Mometasone Furoate, Paramethasone Acetate, Prednicarbate, Prednisolamate Hydrochloride, Prednisolone (Prednisolone Acetate, Prednisolone Hemisuccinate, Prednisolone Hexanoate, Prednisolone Pivalate, Prednisolone Sodium Metasulphobenzoate, Prednisolone Sodium Phosphate, Prednisolone Sodium Succinate, Prednisolone Steaglate, Prednisolone Tebutate), Prednisone (Prednisone Acetate), Prednylidene, Procinonide, Rimexolone, Suprarenal Cortex, Tixocortol Pivalate, Triamcinolone (Triamcinolone Acetonide, Triamcinolone Diacetate and Triamcinolone Hexacetonide).

In another embodiment, the active compound is administered in combination or alternation with one or more other non-steroidal anti-inflammatory drug(s) (NSAIDS). Examples of NSAIDS that can be used in alternation or combination therapy are carboxylic acids, propionic acids, fenamates, acetic acids, pyrazolones, oxicans, alkanones, gold compounds and others that inhibit prostaglandin synthesis, preferably by selectively inhibiting cyclooxygenase-2 (COX-2). Some nonlimiting examples of COX-2 inhibitors are Celebrex (celecoxib) and Vioxx (rofacoxib). Some non-limiting examples of NSAIDS are aspirin (acetylsalicylic acid), Dolobid (diflunisal), Disalcid (salsalate, salicylsalicylate), Trisilate (choline magnesium trisalicylate), sodium salicylate, Cuprimine (penicillamine), Tolectin (tolmetin), ibuprofen (Motrin, Advil, Nuprin Rufen), Naprosyn (naproxen, Anaprox, naproxen sodium), Nalfon (fenoprofen), Orudis (ketoprofen), Ansaid (flurbiprofen), Daypro (oxaprozin), meclofenamate (meclofanamic acid, Meclomen), mefenamic acid, Indocin (indomethacin), Clinoril (sulindac), tolmetin, Voltaren (diclofenac), Lodine (etodolac), ketorolac, Butazolidin (phenylbutazone), Tandearil (oxyphenbutazone), piroxicam (Feldene), Relafen (nabumetone), Myochrysine

(gold sodium thiomalate), Ridaura (auranofin), Solganal (aurothioglucose), acetaminophen, colchicine, Zyloprim (allopurinol), Benemid (probenecid), Anturane (sulfinpyrizone), Plaquenil (hydroxychloroquine), Aceclofenac, Acemetacin, Acetanilide, Actarit, Alclofenac, Alminoprofen, Aloxiprin, Aluminium Aspirin, Amfenac Sodium, Amidopyrine, Aminopropylone, Ammonium Salicylate, Ampiroxicam, Amyl Salicylate, Anirolac, Aspirin, Auranofin, Aurothioglucose, Aurotioprol, Azapropazone, Bendazac (Bendazac Lysine), Benorylate, Benoxaprofen, Benzpiperylone, Benzydamine hydrochloride, Bornyl Salicylate, Bromfenac Sodium, Bufexamac, Bumadizone Calcium, Butibufen Sodium, Capsaicin, Carbaspirin Calcium, Carprofen, Chlorthenoxazin, Choline Magnesium Trisalicylate, Choline Salicylate, Cinmetacin, Clofexamide, Clofezone, Clometacin, Clonixin, Cloracetadol, Cymene, Diacerein, Diclofenac (Diclofenac Diethylammonium Salt, Diclofenac Potassium, Diclofenac Sodium), Diethylamine Salicylate, Diethylsalicylamide, Difenpiramide, Diflunisal, Dipyrone, Droxicam, Epirizole, Etenzamide, Etersalate, Ethyl Salicylate, Etodolac, Etofenamate, Felbinac, Fenbufen, Fenclofenac, Fenoprofen Calcium, Fentiazac, Fepradinol, Feprazone, Floctafenine, Flufenamic, Flunoxaprofen, Flurbiprofen (Flurbiprofen Sodium), Fosfosal, Furprofen, Glafenine, Glucametacin, Glycol Salicylate, Gold Keratinate, Harpagophytum Procumbens, Ibufenac, Ibuprofen, Ibuproxam, Imidazole Salicylate, Indomethacin (Indomethacin Sodium), Indoprofen, Isamifazone, Isonixin, Isoxicam, Kebuzone, Ketoprofen, Ketorolac Trometamol, Lithium Salicylate, Lonazolac Calcium, Lornoxicam, Loxoprofen Sodium, Lysine Aspirin, Magnesium Salicylate, Meclofenamae Sodium, Mefenamic Acid, Meloxicam, Methyl Butetisalicylate, Methyl Gentisate, Methyl Salicylate, Metiazinic Acid, Metifenazone, Mofebutazone, Mofezolac, Morazone Hydrochloride, Mormifumate, Morpholine Salicylate, Nabumetone, Naproxen (Naproxen Sodium), Nifenazone, Niflumic Acid, Nimesulide, Oxametacin, Oxaprozin, Oxindanac, Oxyphenbutazone, Parsalmide, Phenybutazone, Phenyramidol Hydrochloride, Picenadol Hydrochloride, Picolamine Salicylate, Piketoprofen, Pirazolac, Piroxicam, Pirprofen, Pranoprofen, Pranosal, Proglumetacin Maleate, Proquazone, Protizinic Acid, Ramifenazone, Salacetamide, Salamidacetic Acid, Salicylamide, Salix, Salol, Salsalate, Sodium Aurothiomalate, Sodium Gentisate, Sodium Salicylate, Sodium Thiosalicylate, Sulindac, Superoxide Dismutase (Orgotein, Pegorgotein, Sudismase), Suprofen, Suxibuzone, Tenidap Sodium, Tenoxicam, Tetrydamine, Thurfyl Salicylate, Tiaprofenic, Tiaramide Hydrochloride, Tinoridine Hydrochloride, Tolfenamic Acid, Tometin Sodium, Triethanolamine Salicylate, Ufenamate, Zaltoprofen, Zidometacin and Zomepirac Sodium.

VI. Pharmaceutical Compositions

The described derivative of triptolide can be formulated as pharmaceutical compositions and administered for any of the disorders described herein, including autoimmune and inflammitory disorders, in a host, including a human, in any of a variety of forms adapted to the chosen route of administration, including systemically, such as orally, or parenterally, by intravenous, intramuscular, topical, transdermal or subcutaneous routes.

The derivative of triptolide (or prodrug thereof) is included in the pharmaceutically acceptable carrier or diluent in an amount sufficient to deliver to a patient a therapeutically effective amount of compound to treat autoimmune or anti-inflammatory disorders or the symptoms thereof in vivo without causing serious toxic effects in the patient treated.

A preferred dose of the derivatives of triptolide for all of the above-mentioned conditions will be in the range from about 1 to 75 mg/kg, preferably 1 to 20 mg/kg, of body weight per day, more generally 0.1 to about 100 mg per kilogram body weight of the recipient per day. The effective dosage range of the prodrug can be calculated based on the weight of the parent derivative to be delivered.

The derivatives of triptolide are conveniently administered in units of any suitable dosage form, including but not limited to one containing 7 to 3000 mg, preferably 70 to 1400 mg of active ingredient per unit dosage form. An oral dosage of 50-1000 mg is usually convenient, and more typically, 50-500 mg.

Ideally the derivatives of triptolide should be administered to achieve peak plasma concentrations of the active compound of from about 0.2 to 70 μM, preferably about 1.0 to 10 μM. This may be achieved, for example, by the intravenous injection of an appropriate concentration of the active ingredient, optionally in saline, or administered as a bolus of the active ingredient.

The concentration of the derivative of triptolide in the drug composition will depend on absorption, inactivation and excretion rates of the extract as well as other factors known to those of skill in the art. It is to be noted that dosage values will also vary with the severity of the condition to be alleviated. It is to be further understood that for any particular subject, specific dosage regimens should be adjusted over time according to the individual need and the professional judgment of the person administering or

supervising the administration of the compositions, and that the concentration ranges set forth herein are exemplary only and are not intended to limit the scope or practice of the claimed composition. The derivative of triptolide may be administered at once, or may be divided into a number of smaller doses to be administered at varying intervals of time.

A preferred mode of administration of the derivative of triptolide is oral. Oral compositions will generally include an inert diluent or an edible carrier. They may be enclosed in gelatin capsules or compressed into tablets. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form of tablets, troches or capsules. Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition.

The tablets, pills, capsules, troches and the like can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring. When the dosage unit form is a capsule, it can contain, in addition to material of the above type, a liquid carrier such as a fatty oil. In addition, dosage unit forms can contain various other materials which modify the physical form of the dosage unit, for example, coatings of sugar, shellac, or other enteric agents.

The derivative of triptolide can be administered as a component of an elixir, suspension, syrup, wafer, chewing gum or the like. A syrup may contain, in addition to the active compounds, sucrose as a sweetening agent and certain preservatives, dyes and colorings and flavors. The derivatives of triptolide can also be mixed with other active materials that do not impair the desired action, or with materials that supplement the desired action, such as antibiotics, antifungals, anti-inflammatories, or other anti-autoimmune compounds. Solutions or suspensions used for parenteral, intradermal, subcutaneous, or topical application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates

or phosphates and agents for the adjustment of tonicity such as sodium chloride or dextrose. The parental preparation can be enclosed in ampoules, disposable syringes or multiple dose vials made of glass or plastic.

If administered intravenously, preferred carriers are physiological saline or phosphate buffered saline (PBS).

In another embodiment, the derivatives of triptolide are prepared with carriers that will protect the derivatives against rapid elimination from the body, such as a controlled release formulation, including implants and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters and polylactic acid. Methods for preparation of such formulations will be apparent to those skilled in the art.

Liposomal suspensions (including liposomes targeted to infected cells with monoclonal antibodies to viral antigens) are also preferred as pharmaceutically acceptable carriers. These may be prepared according to methods known to those skilled in the art, for example, as described in U.S. Patent No. 4,522,811 (which is incorporated herein by reference in its entirety). For example, liposome formulations may be prepared by dissolving appropriate lipid(s) (such as stearoyl phosphatidyl ethanolamine, stearoyl phosphatidyl choline, arachadoyl phosphatidyl choline, and cholesterol) in an inorganic solvent that is then evaporated, leaving behind a thin film of dried lipid on the surface of the container. An aqueous solution of the active compound or its monophosphate, diphosphate, and/or triphosphate derivatives is then introduced into the container. The container is then swirled by hand to free lipid material from the sides of the container and to disperse lipid aggregates, thereby forming the liposomal suspension.

VII. Synthesis of the Active Compounds

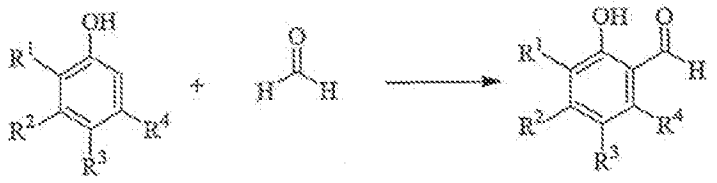
Formylation of a Substituted Phenol:

The starting material for this process is a substituted phenol (A), which can be purchased or can be prepared by any known means to those of ordinary skill in the art. In one embodiment, formylation of the compound of formula (A) results in the formation of an aldehyde of formula (B). The said substituted phenol can be coupled with a

paraformaldehyde in a compatible solvent at a suitable temperature with the appropriate coupling reagent to yield the corresponding aldehyde. Possible coupling reagents are any reagents that promote coupling, including but not limited to $SnCl_4$, BF_3, $AlCl_3$, FeI_3, or $ZnCl_2$, preferably $SnCl_4$.

The formylation reaction can be carried out at any temperature that achieves the desired result, i.e., that is suitable for the reaction to proceed at an acceptable rate without promoting decomposition or excessive side products. The preferred temperature is room temperature.

Any reaction solvent can be selected that can achieve the necessary temperature, can solubilize the reaction components and inert to the reagents. Nonlimiting examples are any aprotic solvent including, but not limited to the alkyl solvents, such as hexane and cyclohexane, toluene, acetone, ethyl acetate, dithianes, triethylamine (TEA), tetrahydrofuran (THF), dioxane, acetonitrile, dichloromethane, dichloroethane, diethyl ether, pyridine, dimethylformamide (DMF), dimethylsulfoxide (DMSO), dimethylacetamide or any combination thereof, though preferably TEA.



A B

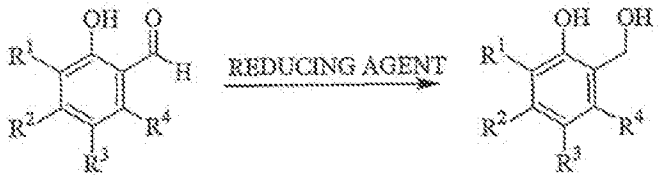
wherein R^1, R^3, and R^4 are selected independently from the groups that include hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, carboxylic acid, amide, nitro, cyano, azide, phosphonyl, phosphinyl, phosphoryl, phosphine, carbamate, ester, alkcarbonyl, carbonyl, a residue of a natural or synthetic amino acid, or carbohydrate or XR^7 (X = O, NR^8 or S).

Reduction of Aldehyde:

In another embodiment of the present invention, reducing the compound of formula B results in the formation of the alcohol of formula C using a reducing agent such

as $NaBH_4$. The reduction reaction can be carried out at any temperature that achieves the desired result, i.e., that is suitable for the reaction to proceed at an acceptable rate without promoting decomposition or excessive side products. The preferred temperature is room temperature.

Any reaction solvent can be selected that can achieve the necessary temperature, can solubilize the reaction components and inert to the reagents. Nonlimiting examples are any aprotic solvent including, but not limited to the alkyl solvents, such as hexane and cyclohexane, toluene, acetone, ethyl acetate, dithianes, triethylamine (TEA), tetrahydrofuran (THF), dioxane, acetonitrile, dichloromethane, dichloroethane, diethyl ether, pyridine, dimethylformamide (DMF), dimethylsulfoxide (DMSO), dimethylacetamide or any combination thereof, though preferably TEA.



B C

wherein R^1, R^3, and R^4 are selected independently from the groups that include hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, carboxylic acid, amide, nitro, cyano, azide, phosphonyl, phosphinyl, phosphoryl, phosphine, carbamate, ester, alkcarbonyl, carbonyl, a residue of a natural or synthetic amino acid, or carbohydrate or XR^7 ($X = O, NR^8$ or S).

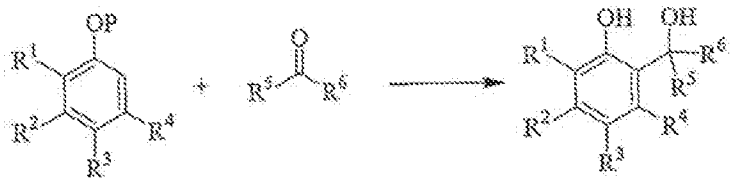
Coupling of a Substituted Phenol:

Alternatively, the substituted phenol can be formed using a ketone. Again, the starting material for this process is a substituted phenol (A), which can be purchased or can be prepared by any known means to those of ordinary skill in the art. In one embodiment, the compound of formula (A), is optionally protected, with an appropriate protecting group, as taught by Greene *et al.* Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991. Coupling of this optionally protected alcohol with an appropriate ketone results in the direct formation of an alcohol of formula (C'). The said substituted phenol can be coupled with the ketone in a compatible solvent at a suitable

temperature with the appropriate base to yield the corresponding aldehyde. Possible coupling reagents are any reagents that promote coupling, including but not limited to lithiates, including, BuLi.

The formylation reaction can be carried out at any temperature that achieves the desired result, i.e., that is suitable for the reaction to proceed at an acceptable rate without promoting decomposition or excessive side products. The preferred temperature is room temperature.

Any reaction solvent can be selected that can achieve the necessary temperature, can solubilize the reaction components and inert to the reagents. Nonlimiting examples are any aprotic solvent including, but not limited to the alkyl solvents, such as hexane and cyclohexane, toluene, acetone, ethyl acetate, dithianes, triethylamine (TEA), tetrahydrofuran (THF), dioxane, acetonitrile, dichloromethane, dichloroethane, diethyl ether, pyridine, dimethylformamide (DMF), dimethylsulfoxide (DMSO), dimethylacetamide or any combination thereof, though preferably TEA.



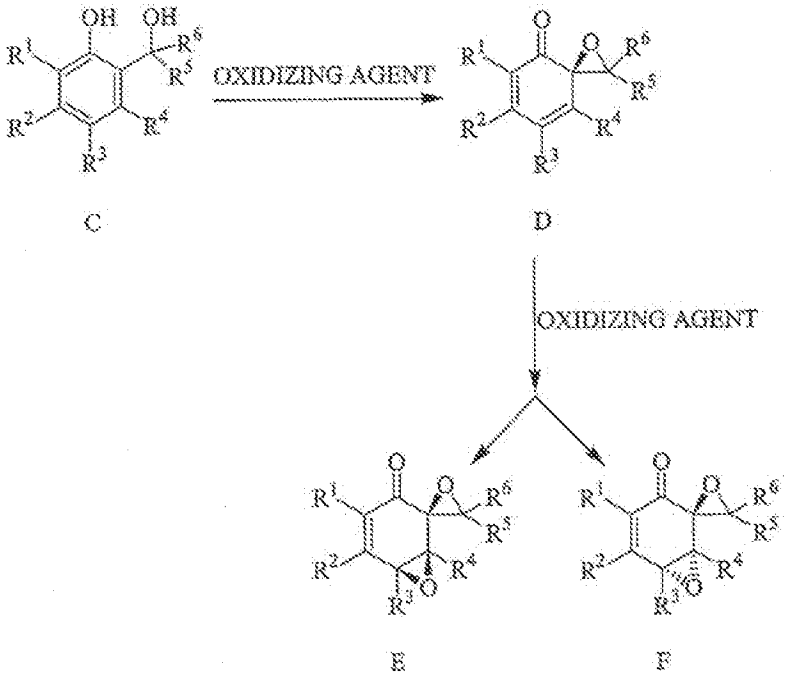
A' C'

Formation of Epoxides:

In yet a further embodiment of the present invention, the epoxidation of the compounds of formula (C) or (C') yields compound (D). In another embodiment of the present invention, the compound of formula (D) is subjected to further oxidation resulting in the compound of formula (E) and (F). The formation of the monoepoxide (D) results from oxidizing the alcohol of formula (C) with an oxidizing agent such as sodium periodate ($NaIO_4$). Upon further oxidation of the monoepoxide (D) using oxidizing agents such as mCPBA give rise to the compound of formula (E) and (F). The oxidation reaction can be carried out at any temperature that achieves the desired result, i.e., that is

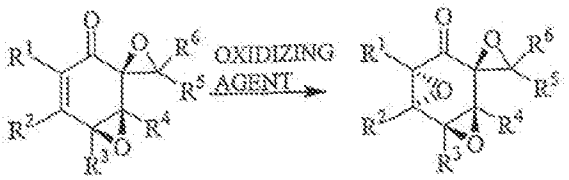
suitable for the reaction to proceed at an acceptable rate without promoting decomposition or excessive side products. The preferred temperature is room temperature.

Any reaction solvent can be selected that can achieve the necessary temperature, can solubilize the reaction components and inert to the reagents. Nonlimiting examples are any aprotic solvent including, but not limited to the alkyl solvents, such as hexane and cyclohexane, toluene, acetone, ethyl acetate, dithianes, triethylamine (TEA), tetrahydrofuran (THF), dioxane, acetonitrile, dichloromethane, dichloroethane, diethyl ether, pyridine, dimethylformamide (DMF), dimethylsulfoxide (DMSO), dimethylacetamide or any combination thereof, though preferably TEA.

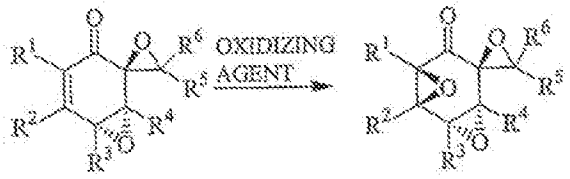


C D E F

It is yet a further embodiment of the present in invention to further oxidize the compounds of formula (E) or (F) to give the stereoselective compounds of formula (G) or (H) respectively. Treating the compounds of formula (E) or (F) with an oxidizing agent such as hydrogen peroxide/NaOH yield the triepoxide (G) or (H) respectively. The oxidation reaction can be carried out at any temperature that achieves the desired result, i.e., that is suitable for the reaction to proceed at an acceptable rate without promoting decomposition or excessive side products. The preferred temperature is room temperature.

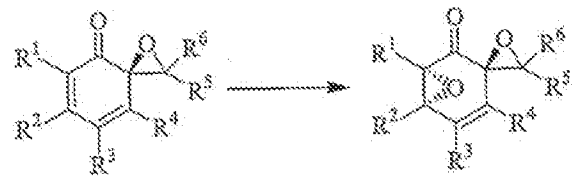


E G



F H

It is also a further embodiment of the present invention to provide for the compound of formula (J). The monoepoxide compound of formula (D) can be further oxidized to give the diepoxide compound of formula (J) using oxidizing agents such as hydrogen peroxide/NaOH. The oxidation reaction can be carried out at any temperature that achieves the desired result, i.e., that is suitable for the reaction to proceed at an acceptable rate without promoting decomposition or excessive side products. The preferred temperature is room temperature.



D J

In another embodiment of the invention, the sulfur analogs are desired. Therefore, the sulfur analogs corresponding to the compounds of the invention can be prepared following the same foregoing general methods, beginning with the corresponding sulfur containing starting material.

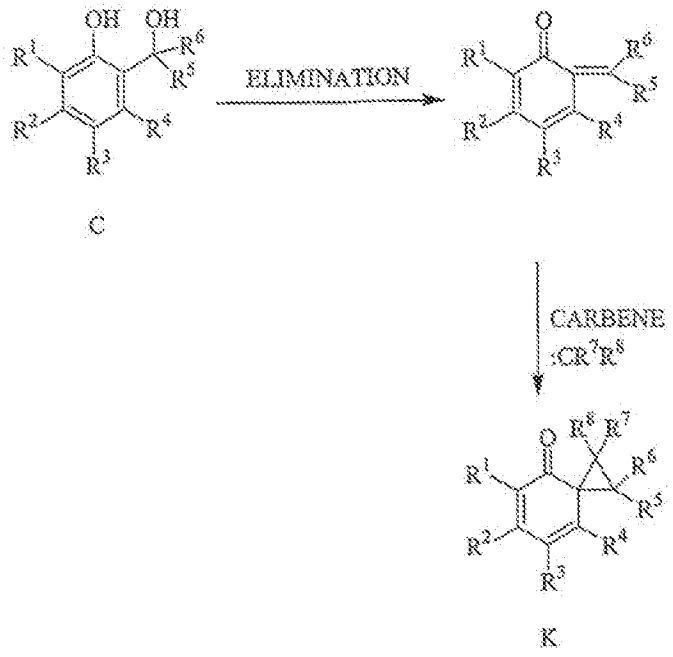
Formation of Cyclopropyls:

In yet a further embodiment of the present invention, the cyclopropanation of the compounds of formula (C) or (C') yields compound (K). The formation of compound (K) results from eliminating the alcohol of formula (C) with an acid to form the alkene. The

alkene can be reacted with the appropriate carbene to form the cyclopropane (K). The appropriate carbene can be made by any means known in the art. In particular, the carbene can be made via α-elimination. For example, dichlorocarbene can be made by treatment of chloroform with a base. Alternatively, the carbene can be made via the Simmons-Smith procedure with Zn-Cu, or Zn and Cu-X (wherein X is a halide), and in particular Zn and Cu-X in the presence of TiX_4. The carbene also can be made by the disintegration of certain types of double bonds, such as the photolysis of a ketene, the isoelectronic decomposition of diazoalkanes, and the decomposition of diazirines (which are isometric with diazoalkanes). Alternatively, ylides, such as $R_2P{=}CR^7$, $R_2S(O)\text{-}CR^7R^8$, such as Trost's and Corey's sulfur ylides, or $R(NR_2)S(O)\text{-}CR^7R^8$, that mimic a carbene, or transition metal-carbene complexes, such as $L_nM{=}CR^7R^8$, wherein M is a metal and L is a ligand, and in particular, when M is Fe, may also be used to form the desired cyclopropane.

Regardless, the coupling reaction with the carbene can be carried out at any temperature that achieves the desired result, i.e., that is suitable for the reaction to proceed at an acceptable rate without promoting decomposition or excessive side products. The preferred temperature is room temperature. In the same way, any of the carbon-carbon pi bonds in compound (C) or (C') can be reacted with the appropriate carbene to form the desired cyclopropane.

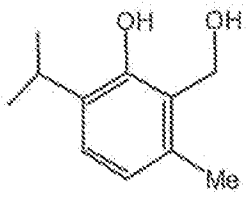
Any reaction solvent can be selected that can achieve the necessary temperature, can solubilize the reaction components and inert to the reagents. Nonlimiting examples are any aprotic solvent including, but not limited to the alkyl solvents, such as hexane and cyclohexane, toluene, acetone, ethyl acetate, dithianes, triethylamine (TEA), tetrahydrofuran (THF), dioxane, acetonitrile, dichloromethane, dichloroethane, diethyl ether, pyridine, dimethylformamide (DMF), dimethylsulfoxide (DMSO), dimethylacetamide or any combination thereof, though preferably TEA.



Example 1

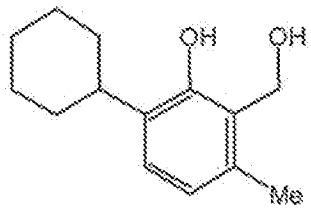
Synthesis of substituted benzyl alcohols.

To a magnetically stirred solution of the phenol (20 mmol) in toluene (10 mL), triethylamine (8 mmol) was added followed by $SnCl_4$ (2 mmol). After stirring for 0.5 h at room temperature, paraformaldehyde (40 mmol) was added and the slurry heated to 95^{0}C for 16 h. The reaction mixture was cooled and poured into water (40 mL) and acidified to pH 2 with 1 N HCl. The aqueous layer was extracted with diethyl ether (3 x 60 mL). The combined organics were washed with brine, dried (sodium sulphate) and concentrated under vacuo. The crude product (**B**) was subjected to reduction with $NaBH_4$ (1.5 equivalents) in MeOH at 0^{0}C. After stirring the reaction for 1 h, the reaction mixture was quenched with a saturated solution of ammonium chloride and acidified to pH 4 with 1 N HCl. MeOH was removed under vacuum and the aqueous layer extracted with ethyl acetate (2 x 50 mL). The combined organics were washed with brine, dried (sodium sulfate) and concentrated under vacuo. Flash chromatography using 1:4::ethyl acetate: hexanes yielded the desired product **C** in moderate yield over 2 steps (35-60%).



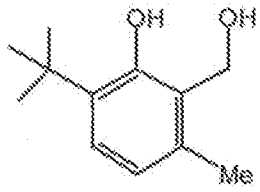
^{1}H NMR ($CDCl_3$): 7.9 (br s, 1H), 7.06 (d, 1H, J = 7.8 Hz), 6.7 (d, 1H, J = 7.8 Hz), 4.94 (s, 2H), 3.3 (m, 1H), 2.24 (s, 3H), 1,24 (d, 6H, J = 6.9 Hz).

^{13}C NMR ($CDCl_3$): 154.02, 133.90, 132.89, 125.62, 122.19, 121.90, 61.38, 26.75, 22.98, 19.40.



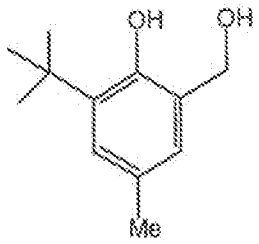
^{1}H NMR ($CDCl_3$): 7.92 (br s, 1H), 7.04 (d, 1H, J = 7.8 Hz), 4.93 (s, 2H), 2.9 (m, 1H), 2.23 (s, 3H), 1.8 (m, 6H), 1.36 (m, 4H).

^{13}C NMR ($CDCl_3$): 153.91, 133.11, 132.85, 126.12, 122.20, 121.90, 61.33, 36.88, 33.5, 27.35, 26.69, 19.39.



^{1}H NMR ($CDCl_3$): 8.1 (br s, 1H), 7.15 (d, 1H, J = 7.8 Hz), 6.67 (d, 1H, J = 7.8 Hz), 4.92 (s, 2H), 2.25 (s, 3H), 1.43 (s, 9H).

^{13}C NMR ($CDCl_3$): 156.17, 135.36, 133.54, 126.43, 123.06, 121.55, 61.26, 34.69, 29.84, 19.26.



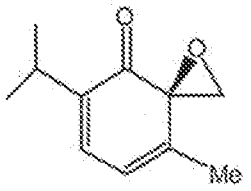
^{1}H NMR ($CDCl_3$): 7.48 (s, 1H), 7.02 (s, 1H), 6.68 (s, 1H), 4.78 (s, 2H), 2.22 (s, 3H), 1.38 (s, 9H).

^{13}C NMR ($CDCl_3$): 153.15, 137.19, 128.41, 127.79, 126.49, 124.80, 65.20, 34.76, 29.81, 20.85

Example 2

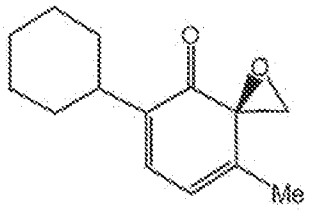
Formation of monoepoxide using sodium periodate:

To a magnetically stirred solution of **C** (2 mmol) in MeOH (12 mL), a solution of $NaIO_4$ (2.2 mmol) in 3 mL water was added dropwise at 0°C. After one minute of stirring a precipitate began to appear. After stirring for another 20 minutes the precipitate was filtered and washed with $CHCl_3$. Water was added and the aqueous layer was extracted with chloroform. The combined organics were washed with brine, dried (sodium sulfate) and concentrated under vacuo. Purification by flash chromatography using 1:7::ethyl acetate: hexanes yielded the desired product (**D**, 80%).



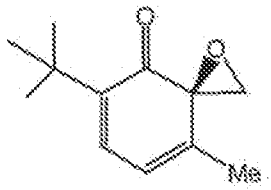
^{1}H NMR ($CDCl_3$): 6.87 (d, 1H, J = 6.6 Hz), 6.3 (m, 1H), 3.22 (d, 1H, J = 8.1 Hz), 3.15 (d, 1H, J = 8.1 Hz), 2.9 (m, 1H), 1.79 (d, 3H, J = 1.5 Hz), 1.08 (d, 3H, J = 2.1 Hz), 1.05 (d, 3H, J = 2.1 Hz).

^{13}C NMR ($CDCl_3$): 195.31, 144.45, 141.75, 135.62, 124.02, 59.27, 58.81, 26.45, 22.14, 21.88, 16.42.



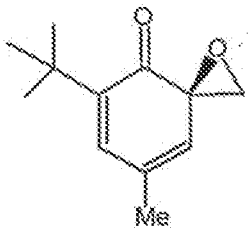
^{1}H NMR ($CDCl_3$): 6.8 (m, 1H), 6.23 (m, 1H), 3.14 (m, 1H), 3.05 (m, 1H), 2.52 (m, 1H), 1.65 (m, 8H), 1.27 (m, 2H), 1.1 (m, 3H)

^{13}C NMR ($CDCl_3$): 195.41, 144.30, 140.89, 136.13, 124.10, 59.12, 58.70, 35.79, 32.56, 32.31, 26.68, 26.59, 26.28, 16.15.



^{1}H NMR ($CDCl_3$): 6.94 (d, 1H, J = 6.3 Hz), 6.27 (d, 1H, J = 6.3 Hz), 3.14 (AB quartet, 2H, J = 8.1 Hz), 1.79 (s, 3H), 1.21 (s, 9H).

^{13}C NMR ($CDCl_3$): 195.07, 145.18, 143.06, 136.44, 123.98, 59.85, 58.44, 34.34, 29.14, 16.19.



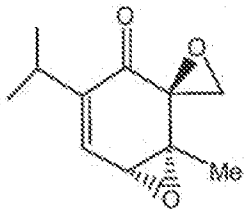
^{1}H NMR ($CDCl_3$): 6.79 (d, 1H, J =2.1 Hz), 5.68 (d, 1H, J = 2.1 Hz), 3.23 (d, 1H, J = 8.1 Hz), 3.01 (d, 1H, J = 8.1 Hz), 1.98 (s, 3H), 1.20 (s, 9H).

^{13}C NMR ($CDCl_3$): 194.42, 144.74, 140.25, 135.79, 130.94, 58.92, 57.26, 34.55, 29.23, 22.00.

Example 3

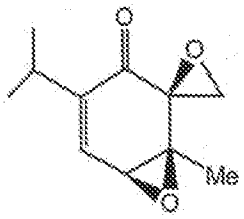
Formation of diepoxides from the monoepoxides using mCPBA:

To a magnetically stirred solution of **D** (1 mmol) in methylene chloride (10 mL), mCPBA was added and the reaction mixture stirred for 14 h. The mixture was diluted with methylene chloride and washed twice with saturated sodium carbonate. The combined organics were washed with brine, dried (sodium sulfate) and concentrated under vacuo. Purification by flash chromatography using 1:7::ethyl acetate:hexanes yielded 2 products that were separated. Stereochemical assignments were made by comparison with literature data. Typically the higher R_F spot was assigned the stereochemistry **F** and the lower R_F spot was assigned the stereochemistry **E**. The combined yield for the reaction was typically 70%.



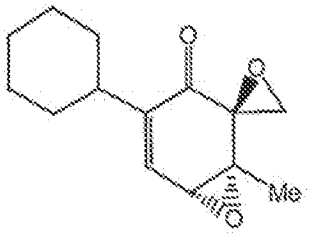
^{1}H NMR ($CDCl_3$): 6.95 (d, 1H, J = 4.5 Hz), 3.46 (d, 1H, J = 4.5 Hz), 3.42 (d, 1H, J = 6.6 Hz), 3.1 (d, 1H, J = 6.6 Hz), 2.85 (m, 1H), 1.31 (s, 3H), 1.04 (d, 3H, J = 5.1 Hz), 1.02 (d, 3H, J = 5.1 Hz).

^{13}C NMR ($CDCl_3$): 190.71, 149.44, 136.89, 61.39, 55.66, 54.43, 50.11, 27.40, 21.67, 21.64, 16.16.



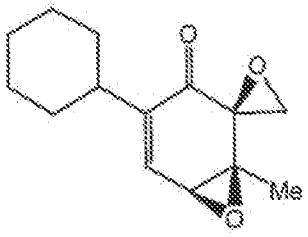
^{1}H NMR ($CDCl_3$): 6.9 (d, 1H, J = 4.5 Hz), 3.51 (d, 1H, J = 4.8 Hz), 2.96 (d, 1H, J = 6.3 Hz), 2.87 (d, 1H, J = 6.3 Hz), 2.79 (m, 1H), 1.32 (s, 3H), 1.06 (d, 3H, J = 6.9 Hz), 0.97 (d, 3H, J = 6.9 Hz).

^{13}C NMR ($CDCl_3$): 191.06, 150.00, 136.40, 59.62, 57.92, 54.55, 52.66, 27.51, 21.69, 21.55, 15.63.



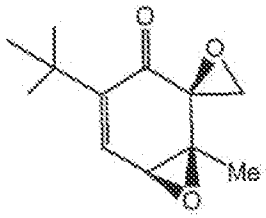
^{1}H NMR ($CDCl_3$): 6.89 (d, 1H, J = 3.3 Hz), 3.44 (d, 1H, J = 3.3 Hz), 3.38 (d, 1H, J = 4.8 Hz), 3.09 (d, 1H, J = 4.8 Hz), 2.49 (m, 1H), 1.71 (m, 5H), 1.3 (s, 3H), 1.33 – 1.03 (m, 5H).

^{13}C NMR ($CDCl_3$): 190.89, 148.72, 137.42, 61.3, 55.59, 54.42, 50.04, 36.85, 32.25, 26.58, 26.56, 26.26, 16.02.



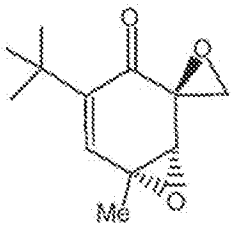
^{1}H NMR ($CDCl_3$): 6.83 (d, 1H, J = 3.6 Hz), 3.5 (d, 1H, J = 3.6 Hz), 2.94 (m, 1H), 2.82 (m, 1H), 2.45 (br t, 1H), 1.73 – 1.52 (m, 5H), 1.13 (s, 3H), 1.26 – 0.96 (m, 5H)

^{13}C NMR ($CDCl_3$): 191.27, 149.21, 136.87, 59.58, 57.76, 54.52, 52.51, 36.85, 32.31, 31.99, 26.50, 26.41, 26.14, 15.39.



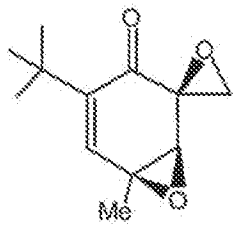
^{1}H NMR ($CDCl_3$): 6.92 (d, 1H, J = 3.3 Hz), 3.49 (d, 1H, J = 3.3 Hz), 2.89 (d, 1H, J = 4.2 Hz), 2.79 (d, 1H, J = 4.2 Hz), 1.31 (s, 3H), 1.14 (s, 9H).

^{13}C NMR ($CDCl_3$): 191.21, 151.52, 136.77, 60.76, 57.35, 54.44, 51.60, 35.05, 28.90, 14.97.



^{1}H NMR ($CDCl_3$): 6.78 (s, 1H), 3.44 (d, 1H, J = 6.6 Hz), 3.21 (s, 1H), 3.03 (d, 1H, J = 6.6 Hz), 1.57 (s, 3H), 1.12 (s, 9H).

^{13}C NMR ($CDCl_3$): 190.07, 149.46, 142.55, 63.23, 54.31, 54.00, 51.34, 35.16, 29.05, 21.07.



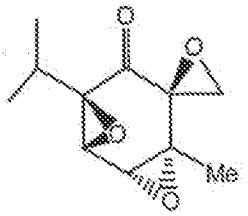
^{1}H NMR ($CDCl_3$): 6.72 (s, 1H), 3.13 (s, 1H), 2.89 (s, 2H), 1.57 (s, 3H), 1.09 (s, 9H).

^{13}C NMR ($CDCl_3$): 190.07, 150.01, 142.08, 60.59, 58.08, 54.85, 52.96, 35.03, 28.98, 21.11.

Example 4

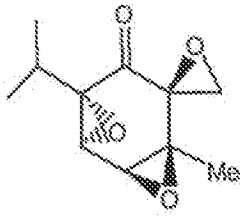
Oxidation of monoepoxides and diepoxides to diepoxides and triepoxides respectively using hydrogen peroxide:

To a magnetically stirred solution of **D** or **F** or **E** (1 mmol) in MeOH (10 mL) at room temperature, 1 N NaOH (0.47 mL) was added followed immediately by the addition of 30 % H_2O_2 (1.5 mmol). After 40 minutes of stirring at room temperature, water was added (40 mL) and the aqueous layer extracted with ethyl acetate (3 x 60 mL). The combined organics were washed with brine, dried (sodium sulfate) and concentrated under vacuo. Flash chromatography using 1;6::ethyl acetate:hexanes yielded the desired product **J**, **H** or **G** respectively in moderate yield (60%).



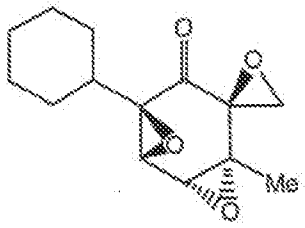
^{1}H NMR ($CDCl_3$): 3.81 (d, 1H, J = 2.4 Hz), 3.62 (d, 1H, J = 2.4 Hz), 3.38 (d, 1H, J = 5.2 Hz), 2.9 (d, 1H, J = 5.2 Hz), 2.39 (m, 1H), 1.23 (s, 3H), 0.96 (d, 3H, J = 6.8 Hz), 0.87(d, 3H, J = 6.8 Hz).

^{13}C NMR ($CDCl_3$): 198.03, 66.15, 59.2, 58.72, 58.5, 56.59, 47.43, 26.02, 18.24, 16.37, 15.62.



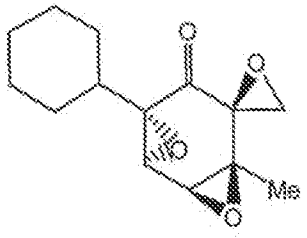
^{1}H NMR ($CDCl_3$): 3.85 (d, 1H, J = 2.8 Hz), 3.67(d, 1H, J = 2.8 Hz), 2.95 (d, 1H, J = 5.2 Hz), 2.74 (d, 1H, J = 5.2 Hz), 2.4 (m, 1H), 1.23 (s, 3H), 0.96 (d, 3H, J = 6.8 Hz), 0.87 (d, 3H, J = 6.8 Hz)

^{13}C NMR ($CDCl_3$): 197.67, 67.22, 60.32, 59.53, 58.43, 50.69, 25.75, 18.11, 16.65, 14.73.



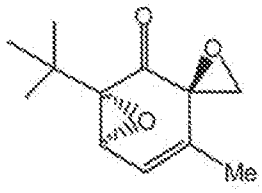
^{1}H NMR ($CDCl_3$): 3.84 (d, 1H, J = 2.8 Hz), 3.61 (d, 1H, J = 2.8 Hz), 3.36 (d, 1H, J = 4.2 Hz), 2.98 (d, 1H, J = 4.2 Hz), 2.12 (m, 1H), 1.74 – 1.58 (m, 5H), 1.23 (s, 3H), 1.28 – 0.87 (m, 5H).

^{13}C NMR ($CDCl_3$): 198.04, 65.85, 59.27, 58.78, 58.44, 56.68, 47.42, 35.07, 28.53, 26.49, 26.24, 26.00, 25.91, 15.57.



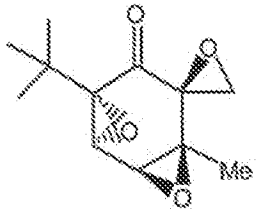
^{1}H NMR ($CDCl_3$): 3.88 (d, 1H, J = 2.8 Hz), 3.66 (d, 1H, J = 2.8 Hz), 2.94 (d, 1H, J = 5.2 Hz), 2.72 (d, 1H, J = 5.2 Hz), 2.15 (m, 1H), 1.73 – 1.63 (m, 5H), 1.22 (s, 3H), 1.28 – 0.89 (m, 5H).

^{13}C NMR ($CDCl_3$): 197.66, 66.93, 60.42, 60.31, 59.48, 58.48, 50.59, 34.64, 28.34, 26.74, 26.16, 25.91, 14.66.



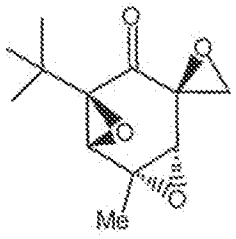
^{1}H NMR ($CDCl_3$): 6.08 (m, 1H), 3.73 (d, 1H, J = 3 Hz), 2.94 (s, 2H), 1.61 (s, 3H), 1.09 (s, 9H).

^{13}C NMR ($CDCl_3$): 200.05, 141.71, 123.21, 64.42, 60.21, 56.4, 52.92, 32.10, 25.76, 15.67.



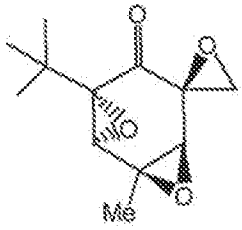
^{1}H NMR ($CDCl_3$): 3.92 (d, 1H, J = 3 Hz), 3.62 (d, 1H, J = 3 Hz), 2.89 (d, 1H, J = 5.1 Hz), 2.67 (d, 1H, J = 5.1 Hz), 1.19 (s, 3H), 1.00 (s, 9H).

^{13}C NMR ($CDCl_3$): 196.86, 68.49, 61.05, 60.19, 59.46, 58.12, 50.22, 32.31, 25.65, 14.47



^{1}H NMR ($CDCl_3$): 3.72 (s, 1H), 2.95 (d, 1H, J = 5.4 Hz), 2.81 (d, 1H, J = 5.4 Hz), 1.66 (s, 3H), 1.01 (s, 9H)

^{13}C NMR ($CDCl_3$): 196.56, 68.30, 64.58, 61.63, 59.03, 58.30, 51.04, 32.43, 25.79, 20.13.



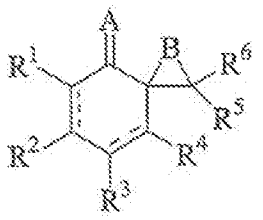
5

^{1}H NMR ($CDCl_3$): 3.72, (d, 1H, J = 1.5 Hz), 3.41 (d, 1H, J = 5.7 Hz), 2.8 (m, 2H), 1.64 (s, 3H), 1.01 (s, 9H).

^{13}C NMR ($CDCl_3$): 196.94, 67.45, 63.68, 60.50, 58.29, 54.5, 50.79, 32.45, 25.92, 19.97.

WE CLAIM:

1. A compound of the formula (I):



(I)

or its pharmaceutically acceptable salt thereof, wherein:

(a) the dotted line indicates the presence of either a single or double bond, wherein the valences of a single bond are completed by hydrogens;

(b) A and B are independently O, S, NR^7 or CR^7R^8;

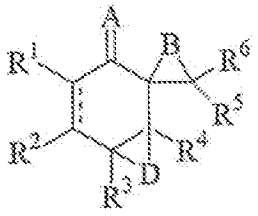
(c) R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, carbonyl, carboxylic acid, ester, carbamate, amide, amine, hydroxyl, alkoxide, nitro, cyano, azide, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, phosphonyl, phosphinyl, phosphoryl, phosphine, a residue of a natural or synthetic amino acid, a residue of a natural or synthetic carbohydrate or XR^9 (wherein X = O, S or NR^{10});

(d) alternatively, one or more of R^1 and R^2, R^2 and R^3, R^3 and R^4, R^4 and R^5, or R^5 and R^6, come together to form a bridged compound, preferably as a 3, 5, 6 or 7 membered ring, to form a cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, heterocyclic, heteroaryl or heteroaromatic; and

(e) each R^7, R^8, R^9 and R^{10} is independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, a residue of a natural or synthetic amino acid or a residue of a natural or synthetic carbohydrate;

optionally in a pharmaceutically acceptable carrier.

2. A compound of the formula (II)



(II)

or its pharmaceutically acceptable salt thereof, wherein:

(a) the dotted line indicates the presence of either a single or double bond, wherein the valences of a single bond are completed by hydrogens;

(b) A, B and D are independently O, S, NR^7 or CR^7R^8;

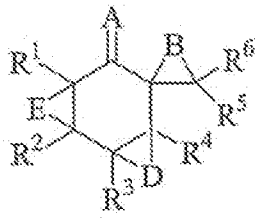
(c) R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, carbonyl, carboxylic acid, ester, carbamate, amide, amine, hydroxyl, alkoxide, nitro, cyano, azide, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, phosphonyl, phosphinyl, phosphoryl, phosphine, a residue of a natural or synthetic amino acid, a residue of a natural or synthetic carbohydrate or XR^9 (wherein X = O, S or NR^{10});

(d) alternatively, one or more of R^1 and R^2, R^2 and R^3, R^3 and R^4, R^4 and R^5, or R^5 and R^6, come together to form a bridged compound, preferably as a 3, 5, 6 or 7 membered ring, to form a cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, heterocyclic, heteroaryl or heteroaromatic; and

(e) each R^7, R^8, R^9 and R^{10} is independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, a residue of a natural or synthetic amino acid or a residue of a natural or synthetic carbohydrate;

optionally in a pharmaceutically acceptable carrier.

3. A compound of the formula (III):



(III)

or its pharmaceutically acceptable salt thereof, wherein:

(a) A, B, D and E are independently O, S, NR^7 or CR^7R^8;

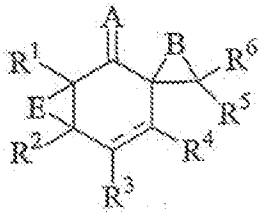
(b) R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, carbonyl, carboxylic acid, ester, carbamate, amide, amine, hydroxyl, alkoxide, nitro, cyano, azide, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, phosphonyl, phosphinyl, phosphoryl, phosphine, a residue of a natural or synthetic amino acid, a residue of a natural or synthetic carbohydrate or XR^9 (wherein X = O, S or NR^{10});

(c) alternatively, one or more of R^1 and R^2, R^2 and R^3, R^3 and R^4, R^4 and R^5, or R^5 and R^6, come together to form a bridged compound, preferably as a 3, 5, 6 or 7 membered ring, to form a cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, heterocyclic, heteroaryl or heteroaromatic; and

(d) each R^7, R^8, R^9 and R^{10} is independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, a residue of a natural or synthetic amino acid or a residue of a natural or synthetic carbohydrate;

optionally in a pharmaceutically acceptable carrier.

4. A compound of the formula (IV):



(IV)

or its pharmaceutically acceptable salt thereof, wherein:

(a) the dotted line indicates the presence of either a single or double bond, wherein the valences of a single bond are completed by hydrogens;

(b) A, B and E are independently O, S, NR^7 or CR^7R^8;

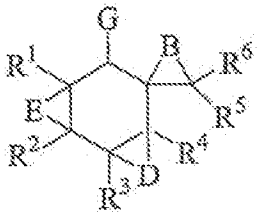
(c) R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, carbonyl, carboxylic acid, ester, carbamate, amide, amine, hydroxyl, alkoxide, nitro, cyano, azide, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, phosphonyl, phosphinyl, phosphoryl, phosphine, a residue of a natural or synthetic amino acid, a residue of a natural or synthetic carbohydrate or XR^9 (wherein X = O, S or NR^{10});

(d) alternatively, one or more of R^1 and R^2, R^2 and R^3, R^3 and R^4, R^4 and R^5, or R^5 and R^6, come together to form a bridged compound, preferably as a 3, 5, 6 or 7 membered ring, to form a cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, heterocyclic, heteroaryl or heteroaromatic; and

(e) each R^7, R^8, R^9 and R^{10} is independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, a residue of a natural or synthetic amino acid or a residue of a natural or synthetic carbohydrate

optionally in a pharmaceutically acceptable carrier.

5. A compound of the formula (V):



(V)

or its pharmaceutically acceptable salt thereof, wherein:

(a) B, D and E are independently O, S, NR^7 or CR^7R^8;

(b) G is OR^{11}, $NR^{11}R^{12}$ or SR^{11};

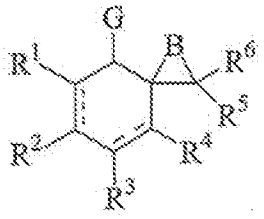
(c) R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, carbonyl, carboxylic acid, ester, carbamate, amide, amine, hydroxyl, alkoxide, nitro, cyano, azide, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, phosphonyl, phosphinyl, phosphoryl, phosphine, a residue of a natural or synthetic amino acid, a residue of a natural or synthetic carbohydrate or XR^9 (wherein X = O, S or NR^{10});

(d) alternatively, one or more of R^1 and R^2, R^2 and R^3, R^3 and R^4, R^4 and R^5, or R^5 and R^6, come together to form a bridged compound, preferably as a 3, 5, 6 or 7 membered ring, to form a cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, heterocyclic, heteroaryl or hetaroaromatic; and

(e) each R^7, R^8, R^9, R^{10}, R^{11} and R^{12} is independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, a residue of a natural or synthetic amino acid or a residue of a natural or synthetic carbohydrate

optionally in a pharmaceutically acceptable carrier.

6. A compound of the formula (VI):



(VI)

or its pharmaceutically acceptable salt thereof, wherein:

(a) the dotted line indicates the presence of either a single or double bond, wherein the valences of a single bond are completed by hydrogens;

(b) B is O, S, NR^7 or CR^7R^8;

(c) G is OR^{11}, $NR^{11}R^{12}$ or SR^{11};

(d) R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl,

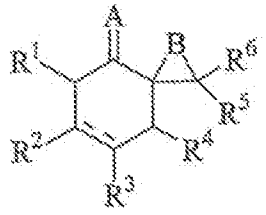
heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, carbonyl, carboxylic acid, ester, carbamate, amide, amine, hydroxyl, alkoxide, nitro, cyano, azide, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, phosphonyl, phosphinyl, phosphoryl, phosphine, a residue of a natural or synthetic amino acid, a residue of a natural or synthetic carbohydrate or XR^9 (wherein X = O, S or NR^{10});

(e) alternatively, one or more of R^1 and R^2, R^2 and R^3, R^3 and R^4, R^4 and R^5, or R^5 and R^6, come together to form a bridged compound, preferably as a 3, 5, 6 or 7 membered ring, to form a cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, heterocyclic, heteroaryl or heteroaromatic; and

(f) each R^7, R^8, R^9, R^{10}, R^{11} and R^{12} is independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, a residue of a natural or synthetic amino acid or a residue of a natural or synthetic carbohydrate;

optionally in a pharmaceutically acceptable carrier.

7. A compound of the formula (VII):



(VII)

or its pharmaceutically acceptable salt thereof, wherein:

(a) the dotted line indicates the presence of either a single or double bond, wherein the valences of a single bond are completed by hydrogens;

(b) A and B are independently O, S, NR^7 or CR^7R^8;

(c) R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, carbonyl, carboxylic acid, ester, carbamate, amide, amine, hydroxyl, alkoxide, nitro, cyano, azide, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, phosphonyl, phosphinyl,

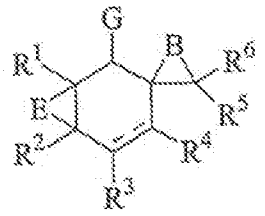
phosphoryl, phosphine, a residue of a natural or synthetic amino acid, a residue of a natural or synthetic carbohydrate or XR^9 (wherein X = O, S or NR^{10});

(d) alternatively, one or more of R^1 and R^2, R^2 and R^3, R^3 and R^4, R^4 and R^5, or R^5 and R^6, come together to form a bridged compound, preferably as a 3, 5, 6 or 7 membered ring, to form a cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, heterocyclic, heteroaryl or heteroaromatic; and

(e) each R^7, R^8, R^9 and R^{10} is independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, a residue of a natural or synthetic amino acid or a residue of a natural or synthetic carbohydrate;

optionally in a pharmaceutically acceptable carrier.

8. A compound of the formula (VIII):



(VIII)

or its pharmaceutically acceptable salt thereof, wherein:

(a) the dotted line indicates the presence of either a single or double bond, wherein the valences of a single bond are completed by hydrogens;

(b) B and E are independently O, S, NR^7 or CR^7R^8;

(c) G is OR^{11}, $NR^{11}R^{12}$ or SR^{11};

(d) R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, carbonyl, carboxylic acid, ester, carbamate, amide, amine, hydroxyl, alkoxide, nitro, cyano, azide, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, phosphonyl, phosphinyl, phosphoryl, phosphine, a residue of a natural or synthetic amino acid, a

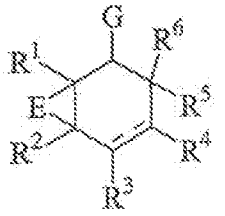
residue of a natural or synthetic carbohydrate or XR^9 (wherein X = O, S or NR^{10});

(e) alternatively, one or more of R^1 and R^2, R^2 and R^3, R^3 and R^4, R^4 and R^5, or R^5 and R^6, come together to form a bridged compound, preferably as a 3, 5, 6 or 7 membered ring, to form a cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, heterocyclic, heteroaryl or heteroaromatic; and

(f) each R^7, R^8, R^9, R^{10}, R^{11} and R^{12} is independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, a residue of a natural or synthetic amino acid or a residue of a natural or synthetic carbohydrate;

optionally in a pharmaceutically acceptable carrier.

9. A compound of the formula (IX):



(IX)

or its pharmaceutically acceptable salt thereof, wherein:

(a) the dotted line indicates the presence of either a single or double bond, wherein the valences of a single bond are completed by hydrogens;

(b) E is O, S, NR^7 or CR^7R^8;

(c) G is OR^{11}, $NR^{11}R^{12}$ or SR^{11};

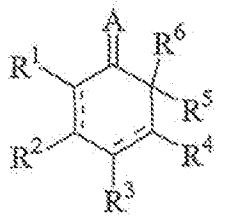
(d) R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, carbonyl, carboxylic acid, ester, carbamate, amide, amine, hydroxyl, alkoxide, nitro, cyano, azide, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, phosphonyl, phosphinyl, phosphoryl, phosphine, a residue of a natural or synthetic amino acid, a residue of a natural or synthetic carbohydrate or XR^9 (wherein X = O, S or NR^{10});

(e) alternatively, one or more of R^1 and R^2, R^2 and R^3, R^3 and R^4, R^4 and R^5, or R^5 and R^6, come together to form a bridged compound, preferably as a 3, 5, 6 or 7 membered ring, to form a cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, heterocyclic, heteroaryl or heteroaromatic; and

(f) each R^7, R^8, R^9, R^{10}, R^{11} and R^{12} is independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, a residue of a natural or synthetic amino acid or a residue of a natural or synthetic carbohydrate;

optionally in a pharmaceutically acceptable carrier.

10. A compound of the formula (X):



(X)

or its pharmaceutically acceptable salt thereof, wherein:

(a) the dotted line indicates the presence of either a single or double bond, wherein the valences of a single bond are completed by hydrogens;

(b) A is O, S, NR^7 or CR^7R^8;

(c) R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, carbonyl, carboxylic acid, ester, carbamate, amide, amine, hydroxyl, alkoxide, nitro, cyano, azide, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, phosphonyl, phosphinyl, phosphoryl, phosphine, a residue of a natural or synthetic amino acid, a residue of a natural or synthetic carbohydrate or XR^9 (wherein X = O, S or NR^{10});

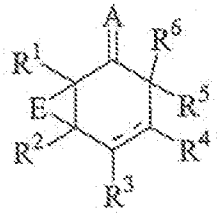
(d) alternatively, one or more of R^1 and R^2, R^2 and R^3, R^3 and R^4, R^4 and R^5, or R^5 and R^6, come together to form a bridged compound, preferably as a 3, 5,

6 or 7 membered ring, to form a cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, heterocyclic, heteroaryl or heteroaromatic; and

(e) each R^7, R^8, R^9 and R^{10} is independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, a residue of a natural or synthetic amino acid or a residue of a natural or synthetic carbohydrate;

optionally in a pharmaceutically acceptable carrier.

11. A compound of the formula (XI):



(XI)

or its pharmaceutically acceptable salt thereof, wherein:

(a) the dotted line indicates the presence of either a single or double bond, wherein the valences of a single bond are completed by hydrogens;

(b) A and E are independently O, S, NR^7 or CR^7R^8;

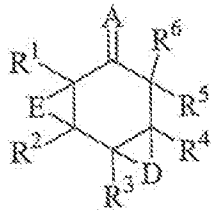
(c) R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, carbonyl, carboxylic acid, ester, carbamate, amide, amine, hydroxyl, alkoxide, nitro, cyano, azide, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, phosphonyl, phosphinyl, phosphoryl, phosphine, a residue of a natural or synthetic amino acid, a residue of a natural or synthetic carbohydrate or XR^9 (wherein X = O, S or NR^{10});

(d) alternatively, one or more of R^1 and R^2, R^2 and R^3, R^3 and R^4, R^4 and R^5, or R^5 and R^6, come together to form a bridged compound, preferably as a 3, 5, 6 or 7 membered ring, to form a cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, heterocyclic, heteroaryl or heteroaromatic; and

(e) each R^7, R^8, R^9 and R^{10} is independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, a residue of a natural or synthetic amino acid or a residue of a natural or synthetic carbohydrate;

optionally in a pharmaceutically acceptable carrier.

12. A compound of the formula (XII):



(XII)

or its pharmaceutically acceptable salt thereof, wherein:

(a) the dotted line indicates the presence of either a single or double bond, wherein the valences of a single bond are completed by hydrogens;

(b) A, D and E are independently O, S, NR^7 or CR^7R^8;

(c) R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, carbonyl, carboxylic acid, ester, carbamate, amide, amine, hydroxyl, alkoxide, nitro, cyano, azide, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, phosphonyl, phosphinyl, phosphoryl, phosphine, a residue of a natural or synthetic amino acid, a residue of a natural or synthetic carbohydrate or XR^9 (wherein X = O, S or NR^{10});

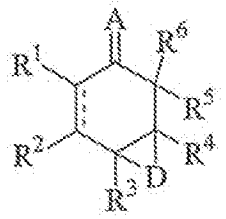
(d) alternatively, one or more of R^1 and R^2, R^2 and R^3, R^3 and R^4, R^4 and R^5, or R^5 and R^6, come together to form a bridged compound, preferably as a 3, 5, 6 or 7 membered ring, to form a cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, heterocyclic, heteroaryl or heteroaromatic; and

(e) each R^7, R^8, R^9 and R^{10} is independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl,

heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, a residue of a natural or synthetic amino acid or a residue of a natural or synthetic carbohydrate;

optionally in a pharmaceutically acceptable carrier.

13. A compound of the formula (XIII):



(XIII)

or its pharmaceutically acceptable salt thereof, wherein:

(a) the dotted line indicates the presence of either a single or double bond, wherein the valences of a single bond are completed by hydrogens;

(b) A and D are independently O, S, NR^7 or CR^7R^8;

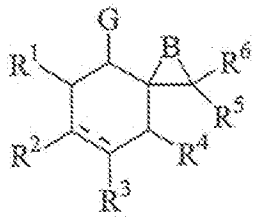
(c) R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, carbonyl, carboxylic acid, ester, carbamate, amide, amine, hydroxyl, alkoxide, nitro, cyano, azide, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, phosphonyl, phosphinyl, phosphoryl, phosphine, a residue of a natural or synthetic amino acid, a residue of a natural or synthetic carbohydrate or XR^9 (wherein X = O, S or NR^{10});

(d) alternatively, one or more of R^1 and R^2, R^2 and R^3, R^3 and R^4, R^4 and R^5, or R^5 and R^6, come together to form a bridged compound, preferably as a 3, 5, 6 or 7 membered ring, to form a cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, heterocyclic, heteroaryl or heteroaromatic; and

(e) each R^7, R^8, R^9 and R^{10} is independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, a residue of a natural or synthetic amino acid or a residue of a natural or synthetic carbohydrate;

optionally in a pharmaceutically acceptable carrier.

14. A compound of the formula (XIV):



(XIV)

or its pharmaceutically acceptable salt thereof, wherein:

(a) the dotted line indicates the presence of either a single or double bond, wherein the valences of a single bond are completed by hydrogens;

(b) B is O, S, NR^7 or CR^7R^8;

(c) G is OR^{11}, $NR^{11}R^{12}$ or SR^{11};

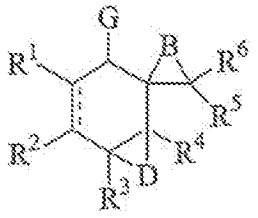
(d) R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, carbonyl, carboxylic acid, ester, carbamate, amide, amine, hydroxyl, alkoxide, nitro, cyano, azide, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, phosphonyl, phosphinyl, phosphoryl, phosphine, a residue of a natural or synthetic amino acid, a residue of a natural or synthetic carbohydrate or XR^9 (wherein X = O, S or NR^{10});

(e) alternatively, one or more of R^1 and R^2, R^2 and R^3, R^3 and R^4, R^4 and R^5, or R^5 and R^6, come together to form a bridged compound, preferably as a 3, 5, 6 or 7 membered ring, to form a cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, heterocyclic, heteroaryl or heteroaromatic; and

(f) each R^7, R^8, R^9, R^{10}, R^{11} and R^{12} is independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, a residue of a natural or synthetic amino acid or a residue of a natural or synthetic carbohydrate;

optionally in a pharmaceutically acceptable carrier.

15. A compound of the formula (XV):



(XV)

or its pharmaceutically acceptable salt thereof, wherein:

(a) the dotted line indicates the presence of either a single or double bond, wherein the valences of a single bond are completed by hydrogens;

(b) B and D are independently O, S, NR^7 or CR^7R^8;

(c) G is OR^{11}, $NR^{11}R^{12}$ or SR^{11};

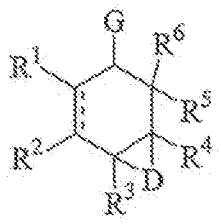
(d) R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, carbonyl, carboxylic acid, ester, carbamate, amide, amine, hydroxyl, alkoxide, nitro, cyano, azide, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, phosphonyl, phosphinyl, phosphoryl, phosphine, a residue of a natural or synthetic amino acid, a residue of a natural or synthetic carbohydrate or XR^9 (wherein X = O, S or NR^{10});

(e) alternatively, one or more of R^1 and R^2, R^2 and R^3, R^3 and R^4, R^4 and R^5, or R^5 and R^6, come together to form a bridged compound, preferably as a 3, 5, 6 or 7 membered ring, to form a cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, heterocyclic, heteroaryl or heteroaromatic; and

(f) each R^7, R^8, R^9, R^{10}, R^{11} and R^{12} is independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, a residue of a natural or synthetic amino acid or a residue of a natural or synthetic carbohydrate;

optionally in a pharmaceutically acceptable carrier.

16. A compound of the formula (XVI):



(XVI)

or its pharmaceutically acceptable salt thereof, wherein:

(a) the dotted line indicates the presence of either a single or double bond, wherein the valences of a single bond are completed by hydrogens;

(b) D is O, S, NR^7 or CR^7R^8;

(c) G is OR^{11}, $NR^{11}R^{12}$ or SR^{11};

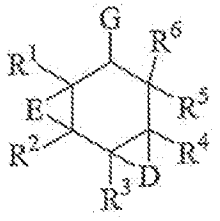
(d) R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, carbonyl, carboxylic acid, ester, carbamate, amide, amine, hydroxyl, alkoxide, nitro, cyano, azide, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, phosphonyl, phosphinyl, phosphoryl, phosphine, a residue of a natural or synthetic amino acid, a residue of a natural or synthetic carbohydrate or XR^9 (wherein X = O, S or NR^{10});

(e) alternatively, one or more of R^1 and R^2, R^2 and R^3, R^3 and R^4, R^4 and R^5, or R^5 and R^6, come together to form a bridged compound, preferably as a 3, 5, 6 or 7 membered ring, to form a cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, heterocyclic, heteroaryl or heteroaromatic; and

(f) each R^7, R^8, R^9, R^{10}, R^{11} and R^{12} is independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, a residue of a natural or synthetic amino acid or a residue of a natural or synthetic carbohydrate;

optionally in a pharmaceutically acceptable carrier.

17. A compound of the formula (XVII):



(XVII)

or its pharmaceutically acceptable salt thereof, wherein:

(a) the dotted line indicates the presence of either a single or double bond, wherein the valences of a single bond are completed by hydrogens;

(b) D and E are independently O, S, NR^7 or CR^7R^8;

(c) G is OR^{11}, $NR^{11}R^{12}$ or SR^{11};

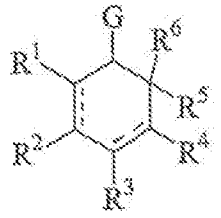
(d) R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, carbonyl, carboxylic acid, ester, carbamate, amide, amine, hydroxyl, alkoxide, nitro, cyano, azide, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, phosphonyl, phosphinyl, phosphoryl, phosphine, a residue of a natural or synthetic amino acid, a residue of a natural or synthetic carbohydrate or XR^9 (wherein X = O, S or NR^{10});

(e) alternatively, one or more of R^1 and R^2, R^2 and R^3, R^3 and R^4, R^4 and R^5, or R^5 and R^6, come together to form a bridged compound, preferably as a 3, 5, 6 or 7 membered ring, to form a cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, heterocyclic, heteroaryl or heteroaromatic; and

(f) each R^7, R^8, R^9, R^{10}, R^{11} and R^{12} is independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, a residue of a natural or synthetic amino acid or a residue of a natural or synthetic carbohydrate;

optionally in a pharmaceutically acceptable carrier.

18. A compound of the formula (XVIII):



(XVIII)

or its pharmaceutically acceptable salt thereof, wherein:

(a) the dotted line indicates the presence of either a single or double bond, wherein the valences of a single bond are completed by hydrogens;

(b) G is OR^{11}, $NR^{11}R^{12}$ or SR^{11};

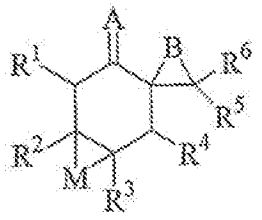
(c) R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, carbonyl, carboxylic acid, ester, carbamate, amide, amine, hydroxyl, alkoxide, nitro, cyano, azide, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, phosphonyl, phosphinyl, phosphoryl, phosphine, a residue of a natural or synthetic amino acid, a residue of a natural or synthetic carbohydrate or XR^9 (wherein X = O, S or NR^{10});

(d) alternatively, one or more of R^1 and R^2, R^2 and R^3, R^3 and R^4, R^4 and R^5, or R^5 and R^6, come together to form a bridged compound, preferably as a 3, 5, 6 or 7 membered ring, to form a cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, heterocyclic, heteroaryl or heteroaromatic; and

(e) each R^7, R^8, R^9, R^{10}, R^{11} and R^{12} is independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, a residue of a natural or synthetic amino acid or a residue of a natural or synthetic carbohydrate;

optionally in a pharmaceutically acceptable carrier.

19. A compound of the formula (XIX):



(XIX)

or its pharmaceutically acceptable salt thereof, wherein:

(a) the dotted line indicates the presence of either a single or double bond, wherein the valences of a single bond are completed by hydrogens;

(b) A, B and M are independently O, S, NR^7 or CR^7R^8;

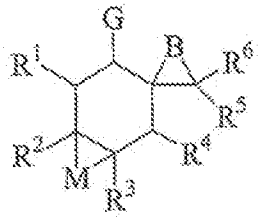
(c) R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, carbonyl, carboxylic acid, ester, carbamate, amide, amine, hydroxyl, alkoxide, nitro, cyano, azide, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, phosphonyl, phosphinyl, phosphoryl, phosphine, a residue of a natural or synthetic amino acid, a residue of a natural or synthetic carbohydrate or XR^9 (wherein X = O, S or NR^{10});

(d) alternatively, one or more of R^1 and R^2, R^2 and R^3, R^3 and R^4, R^4 and R^5, or R^5 and R^6, come together to form a bridged compound, preferably as a 3, 5, 6 or 7 membered ring, to form a cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, heterocyclic, heteroaryl or heteroaromatic; and

(e) each R^7, R^8, R^9 and R^{10} is independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, a residue of a natural or synthetic amino acid or a residue of a natural or synthetic carbohydrate;

optionally in a pharmaceutically acceptable carrier.

20. A compound of the formula (XX):



(XX)

or its pharmaceutically acceptable salt thereof, wherein:

(a) the dotted line indicates the presence of either a single or double bond, wherein the valences of a single bond are completed by hydrogens;

(b) B and M are independently O, S, NR^7 or CR^7R^8;

(c) G is OR^{11}, $NR^{11}R^{12}$ or SR^{11};

(d) R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, carbonyl, carboxylic acid, ester, carbamate, amide, amine, hydroxyl, alkoxide, nitro, cyano, azide, sulfonyl, sulfanyl, sulfinyl, sulfamonyl, phosphonyl, phosphinyl, phosphoryl, phosphine, a residue of a natural or synthetic amino acid, a residue of a natural or synthetic carbohydrate or XR^9 (wherein X = O, S or NR^{10});

(e) alternatively, one or more of R^1 and R^2, R^2 and R^3, R^3 and R^4, R^4 and R^5, or R^5 and R^6, come together to form a bridged compound, preferably as a 3, 5, 6 or 7 membered ring, to form a cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, heterocyclic, heteroaryl or heteroaromatic; and

(f) each R^7, R^8, R^9, R^{10}, R^{11} and R^{12} is independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, alkaryl, arylalkyl, heterocyclic, heteroaryl, heteroaromatic, alkcarbonyl, a residue of a natural or synthetic amino acid or a residue of a natural or synthetic carbohydrate;

optionally in a pharmaceutically acceptable carrier.

21. A pharmaceutical composition for the treatment or prophylaxis of an inflammatory disorder in a host comprising an effective treatment amount of a compound

according to any one of claim 1-20 in combination with one or more anti-inflammatory agent.

22. A pharmaceutical composition for the treatment or prophylaxis of an autoimmune disorder in a host comprising an effective treatment amount of a compound according to any one of claim 1-20 in combination with one or more immunosuppressive agent.

23. A method for the treatment or prophylaxis of an inflammatory disorder in a host comprising administering an effective treatment amount of a compound according to any one of claim 1-20.

24. A method for the treatment or prophylaxis of an autoimmune disorder in a host comprising administering an effective treatment amount of a compound according to any one of claim 1-20.

25. A method for the treatment or prophylaxis of an inflammatory disorder in a host comprising administering an effective treatment amount of the composition of claim 21.

26. A method for the treatment or prophylaxis of an autoimmune disorder in a host comprising administering an effective treatment amount of the composition of claim 22.

27. Use of a compound according to any one of claims 1-20 for the treatment or prophylaxis of an inflammatory disorder in a host.

28. Use of a pharmaceutical composition according to claims 21 for the treatment or prophylaxis of an inflammatory disorder in a host.

29. Use of a pharmaceutical composition according to claims 22 for the treatment or prophylaxis of an autoimmune disorder in a host.

30. Use of a compound according to any one of claims 1-20 in the manufacture of a medicament for the treatment or prophylaxis of an inflammatory disorder in a host.

31. Use of a compound according to any one of claims 1-20 in the manufacture of a medicament for the treatment or prophylaxis of an autoimmune disorder in a host.

32. Use of a pharmaceutical composition according to claims 21 in the manufacture of a medicament for the treatment or prophylaxis of an inflammatory disorder in a host.

33. Use of a pharmaceutical composition according to claims 22 in the manufacture of a medicament for the treatment or prophylaxis of an autoimmune disorder in a host.

FIGURE 1

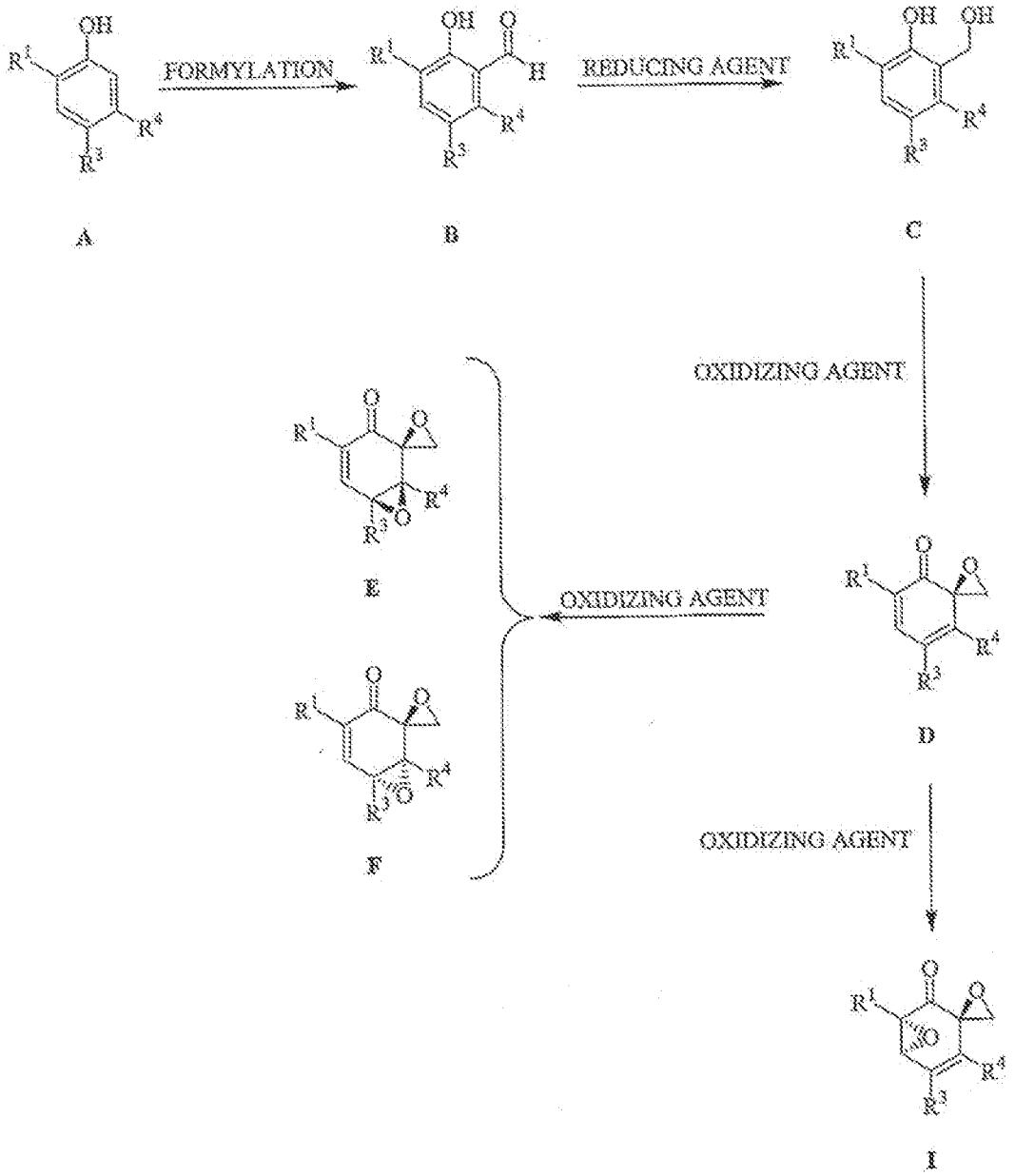
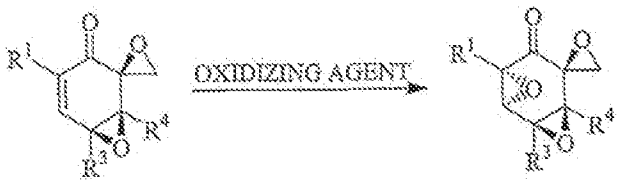

FORMYLATION
REDUCING AGENT
OXIDIZING AGENT
OXIDIZING AGENT
OXIDIZING AGENT
A
B
C
D
E
F
I

FIGURE 2



E G

F H